DESCRIPTION

TRICYCLIC BENZOPYRAN COMPOUND AS ANTI-ARRHYTHMIC AGENTS

Technical Field

The present invention relates to benzopyran derivatives having the prolongation effect on the refractory period, which are used for the treatment of arrhythmia in mammals including human being.

Background Art

As benzopyran derivatives, 4-acylaminobenzopyran derivatives exemplified by Cromakalim have been known (for example, Japanese Patent Laid-open No. Sho 58-67683). These 4-acylaminobenzopyran derivatives exemplified by Cromakalim are known to open ATP sensitive K^+ channel so as to be effective for the treatment of hypertension and asthma, but there has not been any mention as to the treatment of arrhythmia based on the prolongation effect on the refractory period.

In addition, it is reported that 4-aminobenzopyran derivatives that have β3-receptor stimulating action are supposed to be effective for the treatment of corpulence (for example, WO 03/014113), but there has not been any mention as to the treatment of arrhythmia based on the prolongation effect on the refractory period in this document.

Disclosure of Invention

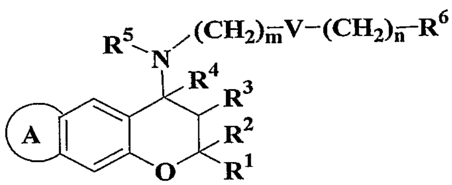
In the meanwhile, conventional anti-arrhythmic agents having the prolongation effect on the refractory period as a main mechanism (such as Class I drugs of anti-arrhythmic agent classification according to Vaughan Williams, or d-sotalol or dofetilide belonging to Class III) have the therapeutic problems in inducing highly dangerous arrhythmia leading to the sudden death from such as *torsades de pointes* among others due to prolongation of action potential in ventricular muscle correlated to the prolongation effect on the refractory period. Thus, treating agents with less adverse effect have been highly desired.

The inventors have investigated compounds having the prolongation effect on the refractory period selective for atrium muscle rather than for ventricular muscle in order to solve the problems, and consequently found that the compound of formula (I) or (II) has the prolongation effect on the refractory period selective for atrium muscle

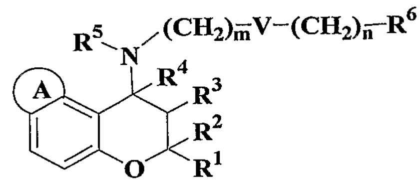
without any influence on the refractory period and action potential in ventricular muscle. Thus, the present invention has been accomplished.

That is, the present invention relates to the following aspects:

(1) A benzopyran derivative of formula (I) or (II), or pharmaceutically acceptable salt thereof



(I)



(II)

wherein

R^1 and R^2 are independently of each other hydrogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), or C_{6-14} aryl group (wherein the aryl group may be arbitrarily substituted with halogen atom, hydroxy group, nitro group, cyano group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group) or C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom));

R^3 is hydroxy group or C_{1-6} alkylcarbonyloxy group, or R^3 forms a bond together with R^4;

R^4 is hydrogen atom, or R^4 forms a bond together with R^3;

m is an integer of 0 to 4;

n is an integer of 0 to 4;

V is a single bond, CR^7R^8 wherein R^7 is

- C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group, C_{1-6} alkoxy group (wherein C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{10} wherein R^{10} is halogen atom; hydroxy group; C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom)); C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom); nitro group; cyano group; formyl group; formamide group; sulfonylamino group;

sulfonyl group; amino group; C_{1-6} alkylamino group; di-C_{1-6} alkylamino group; C_{1-6} alkylcarbonylamino group; C_{1-6} alkylsulfonylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group; di-C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylcarbonyl group; C_{1-6} alkoxycarbonyl group; aminosulfonyl group; C_{1-6} alkylsulfonyl group; carboxy group or C_{6-14} arylcarbonyl group, and when a plurality of R^{10} are present, they may be identical or different from each other); C_{1-6} alkylcarbonyloxy group; nitro group; cyano group; formyl group; formamide group; amino group; C_{1-6} alkylamino group; di-C_{1-6} alkylamino group; C_{1-6} alkylcarbonylamino group; C_{1-6} alkylsulfonylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group; di-C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylcarbonyl group; C_{1-6} alkoxycarbonyl group; aminosulfonyl group; C_{1-6} alkylsulfonyl group; carboxy group or sulfonyl group);

- C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{10} wherein R^{10} has the above-mentioned meaning);
- hydroxy group;
- C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom); or
- nitro group; cyano group; formyl group; formamide group; sulfonylamino group; sulfonyl group; amino group; C_{1-6} alkylamino group; di-C_{1-6} alkylamino group; C_{1-6} alkylcarbonylamino group; C_{1-6} alkylsulfonylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group; di-C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylcarbonyl group; C_{1-6} alkoxycarbonyl group; aminosulfonyl group; C_{1-6} alkylsulfonyl group; carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group (wherein each of the arylcarbonyl group or heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R^{10} wherein R^{10} has the above-mentioned meaning), and

R^8 is

- hydrogen atom,
- C_{1-6} alkyl group (wherein the C_{1-6} alkyl group may be arbitrarily substituted with halogen atom, hydroxy group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10}), C_{1-6} alkylcarbonyloxy group; nitro group; cyano group; formyl group; formamide group; amino group; C_{1-6} alkylamino group; di-C_{1-6} alkylamino group; C_{1-6} alkylcarbonylamino group; C_{1-6} alkylsulfonylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group;

di-C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylcarbonyl group; C_{1-6} alkoxycarbonyl group; aminosulfonyl group; C_{1-6} alkylsulfonyl group; carboxy group or sulfonyl group);
- C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10});
- hydroxy group;
- C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or
- nitro group; cyano group; formyl group; formamide group; sulfonylamino group; sulfonyl group; amino group; C_{1-6} alkylamino group; di-C_{1-6} alkylamino group; C_{1-6} alkylcarbonylamino group; C_{1-6} alkylsulfonylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group; di-C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylcarbonyl group; C_{1-6} alkoxycarbonyl group; aminosulfonyl group; C_{1-6} alkylsulfonyl group; carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group (wherein each of the arylcarbonyl group or heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10}), or
R^7 together with R^8 may represent =O or =S, or
V is NR^9 wherein R^9 is hydrogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), hydroxy group, C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10}), C_{1-6} alkylaminocarbonyl group, di-C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{3-8} cycloalkylcarbonyl group, C_{1-6} alkoxycarbonyl group, C_{1-6} alkylsulfonyl group, carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group), C_{1-6} alkylaminocarbonyl group, di-C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{3-8} cycloalkylcarbonyl group, C_{1-6} alkoxycarbonyl group, C_{1-6} alkylsulfonyl group, C_{6-14} arylsulfonyl group, C_{2-9} heteroarylsulfonyl group (wherein each of the arylsulfonyl group or heteroarylsulfonyl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10}), carboxy group; C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group (wherein each of the arylcarbonyl group or heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10}); or
V is O, S, SO or SO_2;
R^5 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily

substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or hydroxy group); and

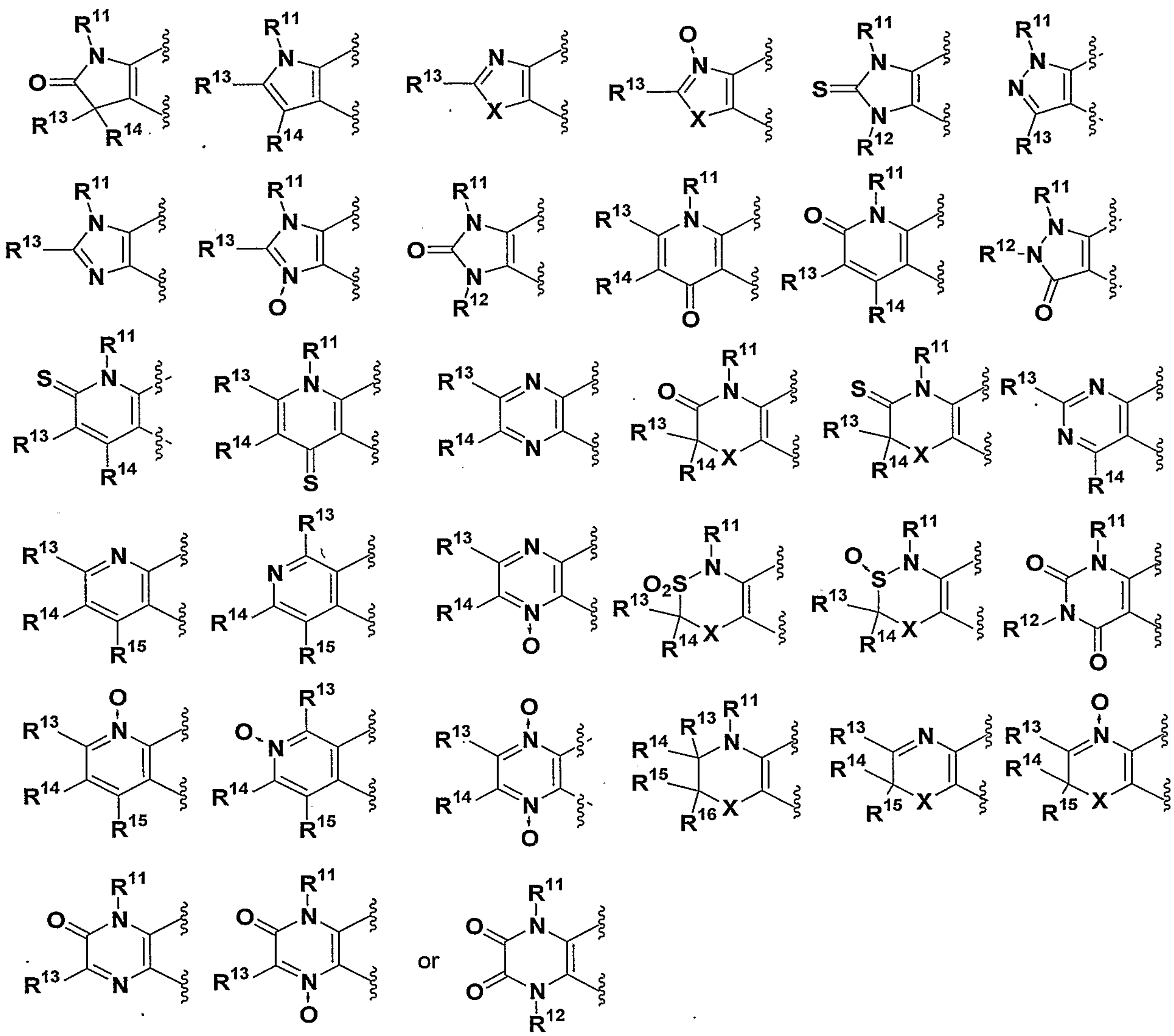
R^6 is

- hydrogen atom,
- C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group),
- C_{3-8} cycloalkyl group, C_{3-8} cycloalkenyl group (wherein the cycloalkyl group or cycloalkenyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group),
- amino group, C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, C_{6-14} arylamino group, C_{2-9} heteroarylamino group (wherein each of the arylamino group or heteroarylamino group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10});
- C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10}); or
- C_{2-9} heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the above-mentioned meaning), hydroxy group, nitro group, cyano group, formyl group, formamide group, amino group, C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, C_{1-6} alkylcarbonylamino group, C_{1-6} alkylsulfonylamino group, aminocarbonyl group, C_{1-6} alkylaminocarbonyl group, di-C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{1-6} alkoxycarbonyl group; aminosulfonyl group, C_{1-6} alkylsulfonyl group, carboxy group or C_{6-14} arylcarbonyl group);

A is 5-, 6- or 7-member ring fused with benzene ring (wherein the 5-, 6- or 7-member

ring may be arbitrarily substituted with 1 to 6 R^{21} wherein R^{21} has the same meaning as R^{10}, and when a plurality of R^{21} are present, they may be identical or different from each other), as constituent atom of the ring, oxygen atom, nitrogen atom or sulfur atom may be contained in the number of 1 to 3 alone or in a combination thereof, the number of unsaturated bond in the ring is 1, 2 or 3 including an unsaturated bond of the benzene ring to be fused, carbon atoms constituting the ring may be carbonyl or thiocarbonyl;

(2) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (1), wherein A is



wherein R^{11} and R^{12} are independently of each other hydrogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy

group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), hydroxy group, C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{19} wherein R^{19} has the same meaning as R^{10}), C_{1-6} alkylaminocarbonyl group, di-C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{3-8} cycloalkylcarbonyl group, C_{1-6} alkoxycarbonyl group, C_{1-6} alkylsulfonyl group, carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group), C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{19} wherein R^{19} has the same meaning as R^{10}), C_{1-6} alkylaminocarbonyl group, di-C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{3-8} cycloalkylcarbonyl group, C_{1-6} alkoxycarbonyl group, C_{1-6} alkylsulfonyl group, C_{6-14} arylsulfonyl group, C_{2-9} heteroarylsulfonyl group (wherein each of the arylsulfonyl group or heteroarylsulfonyl group may be arbitrarily substituted with 1 to 3 R^{19} wherein R^{19} has the same meaning as R^{10}), carboxy group; C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group (wherein each of the arylcarbonyl group or heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R^{19} wherein R^{19} has the same meaning as R^{10}),

R^{13}, R^{14}, R^{15} and R^{16} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, hydroxy group, C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10}), C_{1-6} alkylaminocarbonyl group, di-C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{3-8} cycloalkylcarbonyl group, C_{1-6} alkoxycarbonyl group, C_{1-6} alkylsulfonyl group, carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), carboxy group, amino group, hydroxy group, C_{6-14} aryl group or C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10})), C_{1-6} thioalkoxy group (wherein the thioalkoxy group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), carboxy group, hydroxy group, C_{6-14} aryl group or C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10})), hydroxy group, C_{6-14} aryl group, C_{2-9} heteroaryl

group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10}), C_{1-6} alkylcarbonyloxy group, nitro group, cyano group, formyl group, formamide group, amino group, sulfonyl group, C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, C_{6-14} arylamino group, C_{2-9} heteroarylamino group (wherein each of the arylamino group or heteroarylamino group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10}), C_{1-6} alkylcarbonylamino group, C_{1-6} alkylsulfonylamino group, aminocarbonyl group, C_{1-6} alkylaminocarbonyl group, di-C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{6-14} arylcarbonyl group, C_{2-9} heteroarylcarbonyl group (wherein each of the arylcarbonyl group or heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10}), C_{1-6} alkoxycarbonyl group, aminosulfonyl group, C_{1-6} alkylsulfonyl group, C_{6-14} arylsulfonyl group, C_{2-9} heteroarylsulfonyl group (wherein each of the arylsulfonyl group or heteroarylsulfonyl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10}), carboxy group, sulfonyl group or C_{2-9} heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the above-mentioned meaning), hydroxy group, nitro group, cyano group, formyl group, formamide group, amino group, C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, C_{1-6} alkylcarbonylamino group, C_{1-6} alkylsulfonylamino group, aminocarbonyl group, C_{1-6} alkylaminocarbonyl group, di-C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{1-6} alkoxycarbonyl group, aminosulfonyl group, C_{1-6} alkylsulfonyl group, carboxy group or C_{6-14} arylcarbonyl group),

X is O, S, SO or SO_2;

(3) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (2), wherein R^1 and R^2 are methyl group, R^3 is hydroxy group, and R^4 is hydrogen atom;

(4) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), wherein R^5 is hydrogen atom, m is an integer of 0 to 3 and n is an integer of 0 to 2;

(5) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (4), wherein V is a single bond;

(6) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein m is an integer of 1 to 3, n is 0, and R^6 is C_{6-14} aryl group wherein the aryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10};

(7) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (6), wherein m is 2;

(8) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (7), wherein R^6 is C_{6-14} aryl wherein the aryl group may be arbitrarily substituted with 1 to 3 halogen atom or amino group, and when a plurality of substituents are present, they may be identical or different from each other;

(9) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein m is an integer of 1 to 3, n is 0, and R^6 is C_{2-9} heteroaryl group wherein the heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10};

(10) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (9), wherein m is 2;

(11) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (10), wherein R^6 is 2-pyridyl group, 3-pyridyl group or 4-pyridyl group;

(12) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein m is an integer of 1 to 3, n is 0, and R^6 is C_{2-4} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{3-8} cycloalkyl group, C_{3-8} cycloalkenyl group (wherein the cycloalkyl group or cycloalkenyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), or C_{2-9} heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or

hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), hydroxy group or amino group);

(13) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (12), wherein m is 2;

(14) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (13), wherein R^6 is n-propyl group, i-propyl group, c-pentyl group, c-hexyl group, 1-c-pentenyl group, 2-c-pentenyl group, 3-c-pentenyl group, 1-c-hexenyl group, 2-c-hexenyl group or 3-c-hexenyl group;

(15) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (4), wherein V is CR^7R^8;

(16) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (15), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), or R^7 and R^8 together are =O or =S;

(17) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (16), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group) or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group), or R^7 and R^8 together are =O;

(18) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (17), wherein R^7 is hydroxy group, and R^8 is hydrogen atom;

(19) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (15), wherein m is an integer of 1 to 2, n is 0, and R^6 is C_{6-14} aryl group or C_{2-9} heteroaryl group wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10};

(20) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (19), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the

alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), or R^7 and R^8 together are =O or =S;

(21) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (20), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group) or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group), or R^7 and R^8 together are =O;

(22) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (21), wherein R^7 is hydroxy group, and R^8 is hydrogen atom;

(23) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (22), wherein m is 1, n is 0, and R^6 is C_{6-14} aryl group wherein the aryl group may be arbitrarily substituted with 1 to 3 halogen atom or amino group, when and when a plurality of substituents are present, they may be identical or different from each other;

(24) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (15), wherein m is an integer of 1 to 2, n is 0, and R^6 is C_{1-4} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{3-8} cycloalkyl group, C_{3-8} cycloalkenyl group (wherein the cycloalkyl group or cycloalkenyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino, carboxy group or hydroxy group), or C_{2-9} heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6}

alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group);

(25) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (24), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom), C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), or R^7 and R^8 together are =O or =S;

(26) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (25), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group) or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group), or R^7 and R^8 together are =O;

(27) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (26), wherein R^7 is hydroxy group, and R^8 is hydrogen atom;

(28) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (27), wherein R^6 is n-propyl group, i-propyl group, c-pentyl group, c-hexyl group, 1-c-pentenyl group, 2-c-pentenyl group, 3-c-pentenyl group, 1-c-hexenyl group, 2-c-hexenyl group or 3-c-hexenyl group;

(29) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (15), wherein R^7 and R^8 together are =O or =S, and R^6 is amino group, C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, C_{6-14} arylamino group, C_{2-9} heteroarylamino group (wherein each of the arylamino group or heteroarylamino group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10}), or C_{2-9} heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy

group);

(30) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (4), wherein V is NR^9;

(31) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (30), wherein m is an integer of 1 to 3, n is 0, and R^6 is C_{6-14} aryl group or C_{2-9} heteroaryl group wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10};

(32) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (31), wherein m is 2;

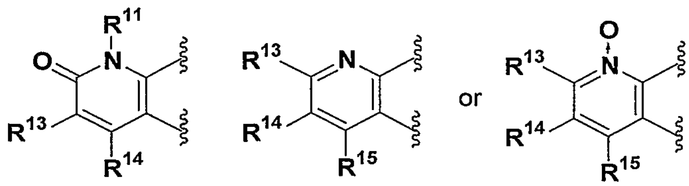
(33) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (30), wherein m is an integer of 1 to 3, n is 0 and R^6 is hydrogen atom, C_{2-4} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{3-8} cycloalkyl group, C_{3-8} cycloalkenyl group (wherein the cycloalkyl group or cycloalkenyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), or C_{2-9} heterocyclyl group (wherein the heterocyclyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group);

(34) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (33), wherein m is 2;

(35) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), which is the compound of formula (I);

(36) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), which is the compound of formula (II);

(37) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (8), (11), (14), (23), (28) or (35), wherein the ring structure of A is



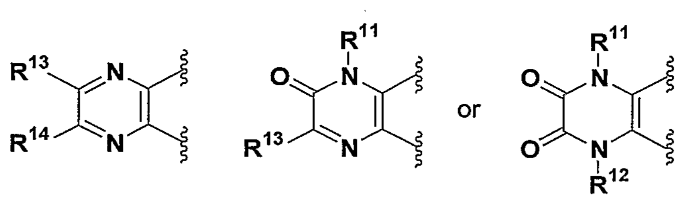
wherein R^{11}, R^{13}, R^{14} and R^{15} have the above-mentioned meanings;

(38) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (37), wherein R^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group or hydroxy group), and R^{13}, R^{14} and R^{15} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{3-8} cycloalkyl group (wherein the cycloalkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group or hydroxy group), C_{1-6} alkoxyl group (wherein the alkoxyl group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{1-6} alkylcarbonyl group, aminocarbonyl group, amino group, carboxy group or cyano group;

(39) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (38), wherein R^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), and R^{13}, R^{14} and R^{15} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), carboxy group, amino group or cyano group;

(40) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (39), wherein R^{11} is hydrogen atom, R^{13} is hydrogen atom, halogen atom, carboxy group or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), R^{14} is hydrogen atom, and R^{15} is hydrogen atom, halogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group);

(41) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (8), (11), (14), (23), (28) or (35), wherein the ring structure of A is



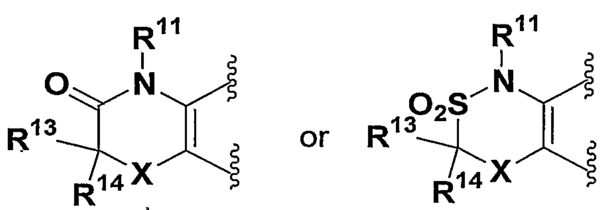
wherein R^{11}, R^{12}, R^{13} and R^{14} have the above-mentioned meanings;

(42) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (41), wherein R^{11} and R^{12} are independently of each other hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group or hydroxy group), and R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or hydroxy group), C_{1-6} alkylcarbonyl group, amino group or cyano group;

(43) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (42), wherein R^{11} and R^{12} are independently of each other hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), and R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), amino group or cyano group;

(44) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (43), wherein R^{11}, R^{12}, R^{13} and R^{14} are hydrogen atom;

(45) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (8), (11), (14), (23), (28) or (35), wherein the ring structure of A is



wherein R^{11}, R^{13} and R^{14} have the above-mentioned meanings;

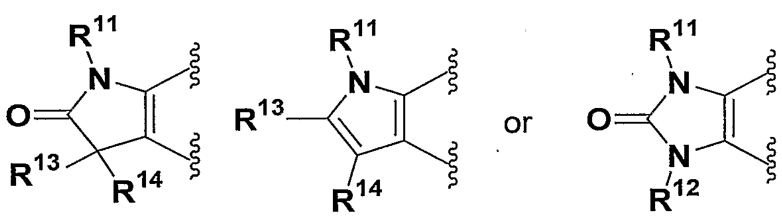
(46) The benzopyran derivative or pharmaceutically acceptable salt thereof as set

forth in (45), wherein R^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group or hydroxy group), R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or hydroxy group), amino group or cyano group, and X is O, S, SO or SO_2;

(47) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (46), wherein R^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), and X is O;

(48) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (47), wherein R^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), R^{13} and R^{14} are hydrogen atom, and X is O;

(49) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (8), (11), (14), (23), (28) or (35), wherein the ring structure of A is



wherein R^{11}, R^{12}, R^{13} and R^{14} have the above-mentioned meanings;

(50) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (49), wherein R^{11} and R^{12} are independently of each other hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group (wherein the aryl group may be arbitrarily substituted with halogen atom, hydroxy group or C_{1-6} alkoxy group (wherein the alkoxy group may

be arbitrarily substituted with halogen atom)), amino group or hydroxy group), and R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or hydroxy group), amino group or cyano group;

(51) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (50), wherein R^{11} and R^{12} are independently of each other hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), and R^{13} and R^{14} are hydrogen atom;

(52) A benzopyran derivative or pharmaceutically acceptable salt thereof which is 2,2,7,9-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 2,2,7-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile, 3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carboxamide, {3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-7-yl}ethanone, 3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinolin-2-ol, 7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carboxylic acid, 4-(benzylamino)-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 4-{[(1,3-benzodioxol-5-yl)methyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 7-chloro-2,2,9-trimethyl-4-[(3-phenylpropyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,

7-chloro-4-{[2-(2-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(4-chlorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
4-{[2-(4-aminophenyl)ethyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(2-hydroxy-2-phenylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-[(2-phenylbutyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
4-{[2-(1,3-benzodioxol-5-yl)ethyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(1-piperidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(1-methyl-2-pyrrolidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
4-[(2-anilinoethyl)amino]-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-({2-[ethyl(3-methylphenyl)amino]ethyl}amino)-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[(1-ethyl-(R)-2-pyrrolidinyl)methyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(2,2-diethoxyethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(3-thienyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(1-pyrazolyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(4-methylpyrazol-1-yl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(4-chloropyrazol-1-yl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(2-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(3-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quin

olin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(4-pyridyl)ethyl}amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-ethylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-isobutylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(cyclopropylmethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-isopentylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(2-cyclopentylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(1-cyclopentenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-[(5-methylhexan-2-yl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[{2-(tetrahydropyran-4-yl)ethyl}amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-[{2-(4-thianyl)ethyl}amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-({[6-(4-chlorophenyl)-3-pyridinyl]methyl}amino)-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
4-[(2-benzofurylmethyl)amino]-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(2-hydroxypentyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
2,2-dimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,

2,2,7,8-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
7,8-diethyl-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
2,2,8-trimethyl-7-phenyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
2,2,7-trimethyl-8-phenyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
2,2,8-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydro-pyrano[2,3-f]benzimidazol-7-one,
7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracen-3-on,
7-hydroxy-4,6,6-trimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracen-3-on,
6,6-dimethyl-8-[(2-phenylethyl)amino]-2,3,4,6,7,8-hexahydro-1,5-dioxa-4-aza-anthracen-7-ol,
7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,6,7,8-tetrahydro-4,5-dioxa-1-aza-anthracen-2-on,
6,6-dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-aza-anthracen-7-ol,
9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-3,7-diol,
7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-6λ5-oxy-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-6λ5-oxy-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-6λ5-oxy-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
4-{[2-(4-fluorophenyl)ethyl]amino}-7-hydroxymethyl-2,2,9-trimethyl-3,4-dihydro-2*H*-pyr

ano[2,3-g]quinolin-3-ol or
2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol;
(53) A benzopyran derivative or pharmaceutically acceptable salt thereof which is
2,2,7-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinolin-2-ol,
7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(2-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(4-chlorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
3-hydroxy-2,2,9-trimethyl-4-[2-(phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carboxylic acid,
4-{[2-(4-aminophenyl)ethyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(2-hydroxy-2-phenylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(1-piperidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(4-chloropyrazol-1-yl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(2-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(3-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-{[2-(4-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-isopentylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(2-cyclopentylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(1-cyclopentenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3

-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-[(2-hydroxypentyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
2,2-dimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,
7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracen-3-on,
7-hydroxy-4,6,6-trimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracen-3-one,
7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-7,8-dihydro-1*H*,6*H*-4,5-dioxa-1-aza-anthracen-2-one,
9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-3,7-diol,
7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-6λ5-oxy-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-6λ5-oxy-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
7-chloro-2,2,9-trimethyl-6λ5-oxy-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
4-{[2-(4-fluorophenyl)ethyl]amino}-7-hydroxymethyl-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol or

2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol;

(54) A pharmaceutical characterized by comprising the benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in any one of (1) to (53) as an active ingredient; and

(55) A pharmaceutical for treating arrhythmia characterized by comprising the benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in any one of (1) to (53) as an active ingredient.

The compound according to the present invention has a strong prolongation effect on the refractory period and it can be used as a drug for treating arrhythmia.

Best Mode for carrying out the Invention

Respective substituents of compounds (I) or (II) according to the present invention are concretely defined below.

In the meanwhile, "n" means normal, "i" means iso, "s" means secondary, "t" means tertiary, "c" means cyclo, "o" means ortho, "m" means meta, "p" means para, "Ph" means phenyl, "Py" means pyridyl, "Bn" means benzyl, "Me" means methyl, "Et" means ethyl, "Pr" means propyl, "Bu" means butyl, "Pen" means pentyl, "Hex" means hexyl, "Ac" means acetyl, "Boc" means tertiary butoxycarbonyl and "MOM" means methoxymethyl in this specification.

Examples of C_{2-4} alkyl group are such as ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl and the like.

Examples of C_{1-4} alkyl group are such as methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl and the like.

Examples of C_{1-6} alkyl group are such as methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, 1-pentyl, 2-pentyl, 3-pentyl, i-pentyl, neopentyl, 2,2-dimethylpropyl, 1-hexyl, 2-hexyl, 3-hexyl, 1-methyl-n-pentyl, 1,1,2-trimethyl-n-propyl, 1,2,2-trimethyl-n-propyl, 3,3-dimethyl-n-butyl and the like.

Preferably, methyl, ethyl, n-propyl, i-propyl, n-butyl, n-pentyl and i-pentyl may be mentioned.

Examples of C_{3-8} cycloalkyl group are such as c-propyl, c-butyl, 1-methyl-c-propyl, 2-methyl-c-propyl, c-pentyl, 1-methyl-c-butyl, 2-methyl-c-butyl, 3-methyl-c-butyl, 1,2-dimethyl-c-propyl, 2,3-dimethyl-c-propyl, 1-ethyl-c-propyl, 2-ethyl-c-propyl, c-hexyl, c-heptyl, c-octyl, 1-methyl-c-hexyl, 2-methyl-c-hexyl, 3-methyl-c-hexyl, 1,2-dimehtyl-c-hexyl, 2,3-dimethyl-c-propyl, 1-ethyl-c-propyl, 1-methyl-c-pentyl, 2-methyl-c-pentyl, 3-methyl-c-pentyl, 1-ethyl-c-butyl, 2-ethyl-c-butyl,

3-ethyl-c-butyl, 1,2-dimethyl-c-butyl, 1,3-dimethyl-c-butyl, 2,2-dimethyl-c-butyl, 2,3-dimethyl-c-butyl, 2,4-dimethyl-c-butyl, 3,3-dimethyl-c-butyl, 1-n-propyl-c-propyl, 2-n-propyl-c-propyl, 1-i-propyl-c-propyl, 2-i-propyl-c-propyl, 1,2,2-trimethyl-c-propyl, 1,2,3-trimethyl-c-propyl, 2,2,3-trimethyl-c-propyl, 1-ethyl-2-methyl-c-propyl, 2-ethyl-1-methyl-c-propyl, 2-ethyl-2-methyl-c-propyl, 2-ethyl-3-methyl-c-propyl, and the like.

Preferably, c-pentyl and c-hexyl may be mentioned.

Examples of C_{3-8} cycloalkenyl group are such as 1-c-pentenyl, 2-c-pentenyl, 3-c-pentenyl, 1-methyl-2-c-pentenyl, 1-methyl-3-c-pentenyl, 2-methyl-1-c-pentenyl, 2-methyl-2-c-pentenyl, 2-methyl-3-c-pentenyl, 2-methyl-4-c-pentenyl, 2-methyl-5-c-pentenyl, 2-methylene-c-pentyl, 3-methyl-1-c-pentenyl, 3-methyl-2-c-pentenyl, 3-methyl-3-c-pentenyl, 3-methyl-4-c-pentenyl, 3-methyl-5-c-pentenyl, 3-methylene-c-pentyl, 1-c-hexenyl, 2-c-hexenyl, 3-c-hexenyl, 1-c-heptynyl, 2-c-heptynyl, 3-c-heptynyl, 4-c-heptynyl, 1-c-octynyl, 2-c-octynyl, 3-c-octynyl, 4-c-octynyl, and the like.

Preferably, 1-c-pentenyl, 2-c-pentenyl, 3-c-pentenyl, 1-c-hexenyl 2-c-hexenyl and 3-c-hexenyl may be mentioned.

Examples of halogen atom are fluorine atom, chlorine atom, bromine atom and iodine atom. Preferably, fluorine atom, chlorine atom and bromine atom may be mentioned.

Examples of C_{1-6} alkoxy group are such as methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, i-butoxy, s-butoxy, t-butoxy, 1-pentyloxy, 2-pentyloxy, 3-pentyloxy, i-pentyloxy, neopentyloxy, 2, 2-dimethylpropoxy, 1-hexyloxy, 2-hexyloxy, 3-hexyloxy, 1-methyl-n-pentyloxy, 1, 1, 2-trimethyl-n-propoxy, 1, 2, 2-trimethyl-n-propoxy, 3, 3-dimethyl-n-butoxy and the like.

Preferably, methoxy, ethoxy, n-propoxy and i-propoxy may be mentioned.

Examples of C_{1-6} thioalkoxy group are such as methylthio, ethylthio, n-propylthio, i-propylthio, c-propylthio, n-butylthio, i-butylthio, s-butylthio, t-butylthio, n-pentylthio, i-pentylthio, neopentylthi, t-pentylthio, n-hexylthio, c-hexylthio and the like.

Examples of C_{1-6} alkylcarbonyloxy group are such as methylcarbonyloxy, ethylcarbonyloxy, n-propylcarbonyloxy, i-propylcarbonyloxy, n-butylcarbonyloxy, i-butylcarbonyloxy, s-butylcarbonyloxy, t-butylcarbonyloxy, 1-pentylcarbonyloxy, 2-pentylcarbonyloxy, 3-pentylcarbonyloxy, i-pentylcarbonyloxy, neopentylcarbonyloxy, t-pentylcarbonyloxy, 1-hexylcarbonyloxy, 2-hexylcarbonyloxy, 3-hexylcarbonyloxy,

1-methyl-n-pentylcarbonyloxy, 1,1,2-trimethyl-n-propylcarbonyloxy, 1,2,2-trimethyl-n-propylcarbonyloxy, 3, 3-dimethyl-n-butylcarbonyloxy and the like.

Preferably, methylcarbonyloxy, ethylcarbonyloxy, n-propylcarbonyloxy, i-propylcarbonyloxy, n-butylcarbonyloxy and t-butylcarbonyloxy may be mentioned.

Examples of C_{6-14} aryl group are such as phenyl, o-biphenylyl, m-biphenylyl, p-biphenylyl, α-naphthyl, β-naphthyl, 1-anthryl, 2-anthryl, 9-anthryl, 1-phenanthryl, 2-phenanthryl, 3-phenanthryl, 4-phenanthryl, 9-phenanthryl and the like.

Preferably, phenyl, o-biphenylyl, m-biphenylyl, p-biphenylyl, α-naphthyl and β-naphthyl may be mentioned.

C_{2-9} heteroaryl group includes C_{2-6} single-ring heterocyclic group with 5- to 7-member ring and C_{5-9} fused double-ring heterocyclic group with member atom number of 8 to 10, which may contain 1 to 3 hetero atoms selected from the group consisting of oxygen atom, nitrogen atom and sulfur atom alone or in a combination.

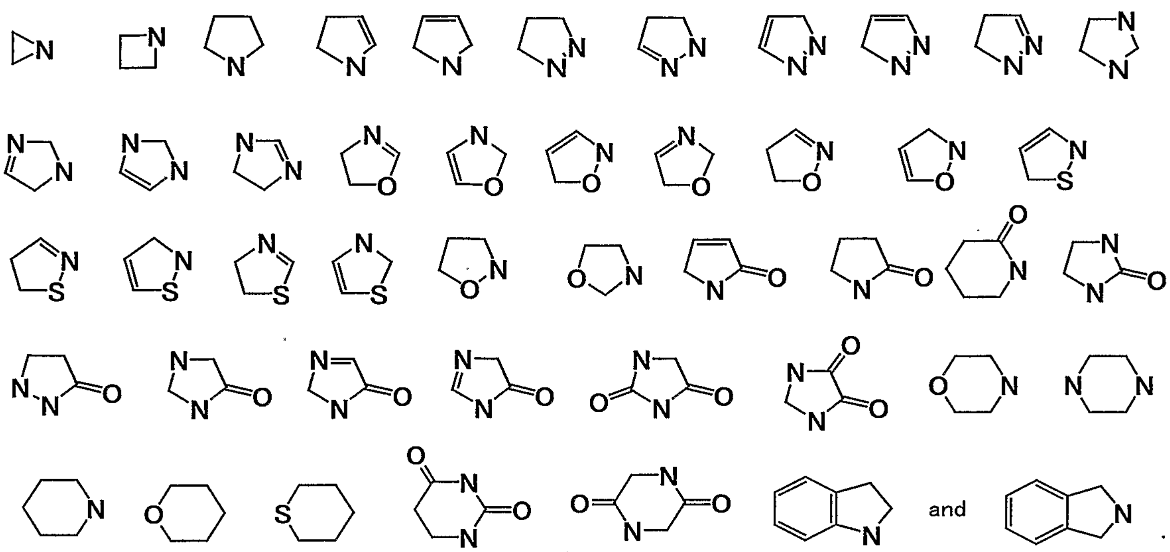
Examples of the C_{2-6} single-ring heterocyclic group with 5- to 7-member ring are such as 2-thienyl group, 3-thienyl group, 2-furyl group, 3-furyl group, 2-pyranyl group, 3-pyranyl group, 4-pyranyl group, 1-pyrrolyl group, 2-pyrrolyl group, 3-pyrrolyl group, 1-imidazolyl group, 2-imidazolyl group, 4-imidazolyl group, 1-pyrazolyl group, 3-pyrazolyl group, 4-pyrazolyl group, 2-thiazolyl group, 4-thiazolyl group, 5-thiazolyl group, 3-isothiazolyl group, 4-isothiazolyl group, 5-isothiazolyl group, 2-oxazolyl group, 4-oxazolyl group, 5-oxazolyl group, 3-isoxazolyl group, 4-isoxazolyl group, 5-isoxazolyl group, 2-pyridyl group, 3-pyridyl group, 4-pyridyl group, 2-pyradinyl group, 2-pyrimidinyl group, 4-pyrimidinyl group, 5-pyrimidinyl group, 3-pyridazinyl group, 4-pyridazinyl group, 2-1,3,4-oxadiazolyl group, 2-1,3,4-thiadiazolyl group, 3-1,2,4-oxadiazolyl group, 5-1,2,4-oxadiazolyl group, 3-1,2,4-thiadiazolyl group, 5-1,2,4-thiadiazolyl group, 3-1,2,5-oxadiazolyl group, 3-1,2,5-thiadiazolyl group and the like.

Examples of the C_{5-9} fused double-ring heterocyclic group with member atom number of 8 to 10 are 2-benzofuranyl group, 3-benzofuranyl group, 4-benzofuranyl group, 5-benzofuranyl group, 6-benzofuranyl group, 7-benzofuranyl group, 1-isobenzofuranyl group, 4-isobenzofuranyl group, 5-isobenzofuranyl group, 2-benzothienyl group, 3-benzothienyl group, 4-benzothienyl group, 5-benzothienyl group, 6-benzothienyl group, 7-benzothienyl group, 1-isobenzothienyl group, 4-isobenzothienyl group, 5-isobenzothienyl group, 2-chromenyl group, 3-chromenyl group, 4-chromenyl group, 5-chromenyl group, 6-chromenyl group, 7-chromenyl group, 8-chromenyl group, 1-indolizinyl group, 2-indolizinyl group, 3-indolizinyl group,

5-indolizinyl group, 6-indolizinyl group, 7-indolizinyl group, 8-indolizinyl group, 1-isoindolyl group, 2-isoindolyl group, 4-isoindolyl group, 5-isoindolyl group, 1-indolyl group, 2-indolyl group, 3-indolyl group, 4-indolyl group, 5-indolyl group, 6-indolyl group, 7-indolyl group, 1-indazolyl group, 2-indazolyl group, 3-indazolyl group, 4-indazolyl group, 5-indazolyl group, 6-indazolyl group, 7-indazolyl group, 1-purinyl group, 2-purinyl group, 3-purinyl group, 6-purinyl group, 7-purinyl group, 8-purinyl group, 2-quinolyl group, 3-quinolyl group, 4-quinolyl group, 5-quinolyl group, 6-quinolyl group, 7-quinolyl group, 8-quinolyl group, 1-isoquinolyl group, 3-isoquinolyl group, 4-isoquinolyl group, 5-isoquinolyl group, 6-isoquinolyl group, 7-isoquinolyl group, 8-isoquinolyl group, 1-phthalazinyl group, 5-phthalazinyl group, 6-phthalazinyl group, 1-2,7-naphthyridinyl group, 3-2,7-naphthyridinyl group, 4-2,7-naphthyridinyl group, 1-2,6-naphthyridinyl group, 3-2,6-naphthyridinyl group, 4-2,6-naphthyridinyl group, 2-1,8-naphthyridinyl group, 3-1,8-naphthyridinyl group, 4-1,8-naphthyridinyl group, 2-1,7-naphthyridinyl group, 3-1,7-naphthyridinyl group, 4-1,7-naphthyridinyl group, 5-1,7-naphthyridinyl group, 6-1,7-naphthyridinyl group, 8-1,7-naphthyridinyl group, 2-1,6-naphthyridinyl group, 3-1,6-naphthyridinyl group, 4-1,6-naphthyridinyl group, 5-1,6-naphthyridinyl group, 7-1,6-naphthyridinyl group, 8-1,6-naphthyridinyl group, 2-1,5-naphthyridinyl group, 3-1,5-naphthyridinyl group, 4-1,5-naphthyridinyl group, 6-1,5-naphthyridinyl group, 7-1,5-naphthyridinyl group, 8-1,5-naphthyridinyl group, 2-quinoxalinyl group, 5-quinoxalinyl group, 6-quinoxalinyl group, 2-quinazolinyl group, 4-quinazolinyl group, 5-quinazolinyl group, 6-quinazolinyl group, 7-quinazolinyl group, 8-quinazolinyl group, 3-cinnolinyl group, 4-cinnolinyl group, 5-cinnolinyl group, 6-cinnolinyl group, 7-cinnolinyl group, 8-cinnolinyl group, 2-pteridinyl group, 4-pteridinyl group, 6-pteridinyl group, 7-pteridinyl group, and the like.

Preferably, 2-pyridyl group, 3-pyridyl group and 4-pyridyl group may be mentioned.

C_{2-9} heterocyclyl group includes single-ring or fused double-ring heterocyclic group composed of 1 or more atoms freely selected from nitrogen atom, oxygen atom and sulfur atom and 2 to 9 carbon atoms, and concretely includes the following groups:



Examples of C_{1-6} alkylamino group are such as methylamino, ethylamino, n-propylamino, i-propylamino, c-propylamino, n-butylamino, i-butylamino, s-butylamino, t-butylamino, c-butylamino, 1-pentylamino, 2-pentylamino, 3-pentylamino, i-pentylamino, neopentylamino, t-pentylamino, c-pentylamino, 1-hexylamino, 2-hexylamino, 3-hexylamino, c-hexylamino, 1-methyl-n-pentylamino, 1,1,2-trimethyl-n-propylamino, 1,2,2-trimethyl-n-propylamino, 3,3-dimethyl-n-butylamino and the like.

Preferably, methylamino, ethylamino, n-propylamino, i-propylamino and n-butylamino may be mentioned.

Examples of di-C_{1-6} alkylamino group are such as dimethylamino, diethylamino, di-n-propylamino, di-i-propylamino, di-c-propylamino, di-n-butylamino, di-i-butylamino, di-s-butylamino, di-t-butylamino, di-c-butylamino, di-1-pentylamino, di-2-pentylamino, di-3-pentylamino, di-i-pentylamino, di-neopentylamino, di-t-pentylamino, di-c-pentylamino, di-1-hexylamino, di-2-hexylamino, di-3-hexylamino, di-c-hexylamino, di-(1-methyl-n-pentyl)amino, di-(1,1,2-trimethyl-n-propyl)amino, di-(1,2,2-trimethyl-n-propyl)amino, di-(3,3-dimethyl-n-butyl)amino, methyl(ethyl)amino, methyl(n-propyl)amino, methyl(i-propyl)amino, methyl(c-propyl)amino, methyl(n-butyl)amino, methyl(i-butyl)amino, methyl(s-butyl)amino, methyl(t-butyl)amino, methyl(c-butyl)amino, ethyl(n-propyl)amino, ethyl(i-propyl)amino, ethyl(c-propyl)amino, ethyl(n-butyl)amino, ethyl(i-butyl)amino, ethyl(s-butyl)amino, ethyl(t-butyl)amino, ethyl(c-butyl)amino, n-propyl(i-propyl)amino, n-propyl(c-propyl)amino, n-propyl(n-butyl)amino, n-propyl(i-butyl)amino, n-propyl(s-butyl)amino, n-propyl(t-butyl)amino, n-propyl(c-butyl)amino,

i-propyl(c-propyl)amino, i-propyl(n-butyl)amino, i-propyl(i-butyl)amino, i-propyl(s-butyl)amino, i-propyl(t-butyl)amino, i-propyl(c-butyl)amino, c-propyl(n-butyl)amino, c-propyl(i-butyl)amino, c-propyl(s-butyl)amino, c-propyl(t-butyl)amino, c-propyl(c-butyl)amino, n-butyl(i-butyl)amino, n-butyl(s-butyl)amino, n-butyl(t-butyl)amino, n-butyl(c-butyl)amino, i-butyl(s-butyl)amino, i-butyl(t-butyl)amino, i-butyl(c-butyl)amino, s-butyl(t-butyl)amino, s-butyl(c-butyl)amino, t-butyl(c-butyl)amino and the like.

Preferably, dimethylamino, diethylamino, di-n-propylamino, di-i-propylamino and di-n-butylamino may be mentioned.

Examples of C_{1-6} alkylcarbonylamino group are such as methylcarbonylamino, ethylcarbonylamino, n-propylcarbonylamino, i-propylcarbonylamino, n-butylcarbonylamino, i-butylcarbonylamino, s-butylcarbonylamino, t-butylcarbonylamino, 1-pentylcarbonylamino, 2-pentylcarbonylamino, 3-penylcarbonylamino, i-pentylcarbonylamino, neopentylcarbonylamino, t-pentylcarbonylamino, 1-hexylcarbonylamino, 2-hexylcarbonylamino, 3-hexylcarbonylamino and the like.

Preferably, methylcarbonylamino, ethylcarbonylamino, n-propylcarbonylamino, i-propylcarbonylamino and n-butylcarbonylamino may be mentioned.

Examples of C_{1-6} alkylsulfonylamino group are such as methylsulfonylamino, ethylsulfonylamino, n-propylsulfonylamino, i-propylsulfonylamino, n-butylsulfonylamino, i-butylsulfonylamino, s-butylsulfonylamino, t-butylsulfonylamino, 1-pentylsulfonylamino, 2-pentylsulfonylamino, 3-pentylsulfonylamino, i-pentylsulfonylamino, neopentylsulfonylamino, t-pentylsulfonylamino, 1-hexylsulfonylamino, 2-hexylsulfonylamino, 3-hexylsulfonylamino and the like.

Preferably, methylsulfonylamino, ethylsulfonylamino, n-propylsulfonylamino, i-propylsulfonylamino and n-butylsulfonylamino may be mentioned.

Examples of C_{1-6} alkylaminocarbonyl group are such as methylaminocarbonyl, ethylaminocarbonyl, n-propylaminocarbonyl, i-propyl-aminocarbonyl, n-butylaminocarbonyl, i-butylaminocarbonyl, s-butylaminocarbonyl, t-butylaminocarbonyl, 1-pentylaminocarbonyl, 2-pentylaminocarbonyl, 3-pentyl-aminocarbonyl, i-pentylaminocarbonyl, neopentylaminocarbonyl, t-pentylamino-carbonyl, 1-hexylaminocarbonyl, 2-hexylaminocarbonyl, 3-hexylaminocarbonyl and the like.

Preferably, methylaminocarbonyl, ethylaminocarbonyl, n-propylaminocarbonyl, i-propylaminocarbonyl and n-butylaminocarbonyl may be mentioned.

Examples of di-C_{1-6} alkylaminocarbonyl group are such as dimethylaminocarbonyl, diethylaminocarbonyl, di-n-propylaminocarbonyl, di-i-propylaminocarbonyl, di-c-propylaminocarbonyl, di-n-butylaminocarbonyl, di-i-butylaminocarbonyl, di-s-butylaminocarbonyl, di-t-butylaminocarbonyl, di-c-butylaminocarbonyl, di-1-pentylaminocarbonyl, di-2-pentylaminocarbonyl, di-3-pentylaminocarbonyl, di-i-pentylaminocarbonyl, di-neopentylaminocarbonyl, di-t-pentylaminocarbonyl, di-c-pentylaminocarbonyl, di-1-hexylaminocarbonyl, di-2-hexylaminocarbonyl, di-3-hexylaminocarbonyl, di-c-hexylaminocarbonyl, di-(1-methyl-n-pentyl)aminocarbonyl, di-(1,1,2-trimethyl-n-propyl)aminocarbonyl, di-(1,2,2-trimethyl-n-propyl)aminocarbonyl, di-(3,3-dimethyl-n-butyl)aminocarbonyl, methyl(ethyl)aminocarbonyl, methyl(n-propyl)aminocarbonyl, methyl(i-propyl)aminocarbonyl, methyl(c-propyl)aminocarbonyl, methyl(n-butyl)aminocarbonyl, methyl(i-butyl)aminocarbonyl, methyl(s-butyl)aminocarbonyl, methyl(t-butyl)aminocarbonyl, methyl(c-butyl)aminocarbonyl, ethyl(n-propyl)aminocarbonyl, ethyl(i-propyl)aminocarbonyl, ethyl(c-propyl)aminocarbonyl, ethyl(n-butyl)aminocarbonyl, ethyl(i-butyl)aminocarbonyl, ethyl(s-butyl)aminocarbonyl, ethyl(t-butyl)aminocarbonyl, ethyl(c-butyl)aminocarbonyl, n-propyl(i-propyl)aminocarbonyl, n-propyl(c-propyl)aminocarbonyl, n-propyl(n-butyl)aminocarbonyl, n-propyl(i-butyl)aminocarbonyl, n-propyl(s-butyl)aminocarbonyl, n-propyl(t-butyl)aminocarbonyl, n-propyl(c-butyl)aminocarbonyl, i-propyl(c-butyl)aminocarbonyl, i-propyl(n-butyl)aminocarbonyl, i-propyl(i-butyl)aminocarbonyl, i-propyl(s-butyl)aminocarbonyl, i-propyl(t-butyl)aminocarbonyl, i-propyl(c-butyl)aminocarbonyl, c-propyl(n-butyl)aminocarbonyl, c-propyl(i-butyl)aminocarbonyl, c-propyl(s-butyl)aminocarbonyl, c-propyl(t-butyl)aminocarbonyl, c-propyl(c-butyl)aminocarbonyl, n-butyl(i-butyl)aminocarbonyl, n-butyl(s-butyl)aminocarbonyl, n-butyl(t-butyl)aminocarbonyl, n-butyl(c-butyl)aminocarbonyl, i-butyl(s-butyl)aminocarbonyl, i-butyl(t-butyl)aminocarbonyl, i-butyl(t-butyl)aminocarbonyl, i-butyl(c-butyl)aminocarbonyl, s-butyl(t-butyl)aminocarbonyl, s-butyl(c-butyl)aminocarbonyl, t-butyl(c-butyl)aminocarbonyl, and the like.

Preferably, dimethylaminocarbonyl, diethylaminocarbonyl, di-n-propylaminocarbonyl, di-i-propylaminocarbonyl, di-c-propylaminocarbonyl and

di-n-butylaminocarbonyl may be mentioned.

Examples of C_{1-6} alkylcarbonyl group are such as methylcarbonyl, ethylcarbonyl, n-propylcarbonyl, i-propylcarbonyl, n-butylcarbonyl, i-butylcarbonyl, s-butylcarbonyl, t-butylcarbonyl, 1-pentylcarbonyl, 2-pentylcarbonyl, 3-pentylcarbonyl, i-pentylcarbonyl, neopentylcarbonyl, t-pentylcarbonyl, 1-hexylcarbonyl, 2-hexylcarbonyl, 3-hexylcarbonyl and the like.

Preferably, methylcarbonyl, ethylcarbonyl, n-propylcarbonyl, i-propylcarbonyl and n-butylcarbonyl may be mentioned.

Examples of C_{3-8} cycloalkylcarbonyl group are such as c-propylcarbonyl, c-butylcarbonyl, 1-methyl-c-propylcarbonyl, 2-methyl-c-propylcarbonyl, c-pentylcarbonyl, 1-methyl-c-butylcarbonyl, 2-methyl-c-butylcarbonyl, 3-methyl-c-butylcarbonyl, 1,2-dimethyl-c-propylcarbonyl, 2,3-dimethyl-c-propylcarbonyl, 1-ethyl-c-propylcarbonyl, 2-ethyl-c-propylcarbonyl, c-hexylcarbonyl, c-heptylcarbonyl, c-octylcarbonyl, 1-methyl-c-hexylcarbonyl, 2-methyl-c-hexylcarbonyl, 3-methyl-c-hexylcarbonyl, 1,2-dimehtyl-c-hexylcarbonyl, 2,3-dimethyl-c-propylcarbonyl, 1-ethyl-c-propylcarbonyl, 1-methyl-c-pentylcarbonyl, 2-methyl-c-pentylcarbonyl, 3-methyl-c-pentylcarbonyl, 1-ethyl-c-butylcarbonyl, 2-ethyl-c-butylcarbonyl, 3-ethyl-c-butylcarbonyl, 1,2-dimethyl-c-butylcarbonyl, 1,3-dimethyl-c-butylcarbonyl, 2,2-dimethyl-c-butylcarbonyl, 2,3-dimethyl-c-butylcarbonyl, 2,4-dimethyl-c-butylcarbonyl, 3,3-dimethyl-c-butylcarbonyl, 1-n-propyl-c-propylcarbonyl, 2-n-propyl-c-propylcarbonyl, 1-i-propyl-c-propylcarbonyl, 2-i-propyl-c-propylcarbonyl, 1,2,2-trimethyl-c-propylcarbonyl, 1,2,3-trimethyl-c-propylcarbonyl, 2,2,3-trimethyl-c-propylcarbonyl, 1-ethyl-2-methyl-c-propylcarbonyl, 2-ethyl-1-methyl-c-propylcarbonyl, 2-ethyl-2-methyl-c-propylcarbonyl, 2-ethyl-3-methyl-c-propylcarbonyl, and the like.

Preferably, c-pentylcarbonyl and c-hexylcarbonyl may be mentioned.

Examples of C_{1-6} alkoxycarbonyl group are such as methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, i-propoxycarbonyl, n-butoxycarbonyl, i-butoxycarbonyl, s-butoxycarbonyl, t-butoxycarbonyl, 1-pentyloxycarbonyl, 2-pentyloxycarbonyl, 3-pentyloxycarbonyl, i-pentyloxycarbonyl, neopentyloxycarbonyl, t-pentyloxycarbonyl, 1-hexyloxycarbonyl, 2-hexyloxycarbonyl, 3-hexyloxycarbonyl and the like.

Preferably, methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, i-propoxycarbonyl, n-butoxycarbonyl, i-butoxycarbonyl, s-butoxycarbonyl and

t-butoxycarbonyl may be mentioned.

Examples of C_{1-6} alkylsulfonyl group are such as methanesulfonyl, trifluoromethanesulfonyl, ethanesulfonyl and the like.

Examples of C_{6-14} arylcarbonyl group are such as benzoyl, o-biphenylylcarbonyl, m-biphenylylcarbonyl, p-biphenylylcarbonyl, α-naphthylcarbonyl, β-naphthylcarbonyl, 1-anthrylcarbonyl, 2-anthrylcarbonyl, 9-anthrylcarbonyl, 1-phenanthrylcarbonyl, 2-phenanthrylcarbonyl, 3-phenanthrylcarbonyl, 4-phenanthrylcarbonyl, 9-phenanthrylcarbonyl and the like.

Preferably, benzoyl, o-biphenylylcarbonyl, m-biphenylylcarbonyl, p-biphenylylcarbonyl, α-naphthylcarbonyl and β-naphthylcarbonyl may be mentioned.

C_{2-9} heteroarylcarbonyl group includes C_{2-6} single-ring heterocyclic carbonyl group with 5- to 7-member ring and C_{5-9} fused double-ring heterocyclic carbonyl group with member atom number of 8 to 10, which may contain 1 to 3 hetero atoms selected from the group consisting of oxygen atom, nitrogen atom and sulfur atom alone or in a combination.

Examples of the C_{2-6} single-ring heterocyclic carbonyl group with 5- to 7-member ring are such as 2-thienylcarbonyl group, 3-thienylcarbonyl group, 2-furylcarbonyl group, 3-furylcarbonyl group, 2-pyranylcarbonyl group, 3-pyranylcarbonyl group, 4-pyranylcarbonyl group, 1-pyrrolylcarbonyl group, 2-pyrrolylcarbonyl group, 3-pyrrolylcarbonyl group, 1-imidazolylcarbonyl group, 2-imidazolylcarbonyl group, 4-imidazolylcarbonyl group, 1-pyrazolylcarbonyl group, 3-pyrazolylcarbonyl group, 4-pyrazolylcarbonyl group, 2-thiazolylcarbonyl group, 4-thiazolylcarbonyl group, 5-thiazolylcarbonyl group, 3-isothiazolylcarbonyl group, 4-isothiazolylcarbonyl group, 5-isothiazolylcarbonyl group, 2-oxazolylcarbonyl group, 4-oxazolylcarbonyl group, 5-oxazolylcarbonyl group, 3-isoxazolylcarbonyl group, 4-isoxazolylcarbonyl group, 5-isoxazolylcarbonyl group, 2-pyridylcarbonyl group, 3-pyridylcarbonyl group, 4-pyridylcarbonyl group, 2-pyradinylcarbonyl group, 2-pyrimidinylcarbonyl group, 4-pyrimidinylcarbonyl group, 5-pyrimidinylcarbonyl group, 3-pyridazinylcarbonyl group, 4-pyridazinylcarbonyl group, 2-1,3,4-oxadiazolylcarbonyl group, 2-1,3,4-thiadiazolylcarbonyl group, 3-1,2,4-oxadiazolylcarbonyl group, 5-1,2,4-oxadiazolylcarbonyl group, 3-1,2,4-thiadiazolylcarbonyl group, 5-1,2,4-thiadiazolylcarbonyl group, 3-1,2,5-oxadiazolylcarbonyl group, 3-1,2,5-thiadiazolylcarbonyl group and the like.

Examples of the C_{5-9} fused double-ring heterocyclic carbonyl group with member atom number of 8 to 10 are 2-benzofuranylcarbonyl group,

3-benzofuranylcarbonyl group, 4-benzofuranylcarbonyl group, 5-benzofuranylcarbonyl group, 6-benzofuranylcarbonyl group, 7-benzofuranylcarbonyl group, 1-isobenzofuranylcarbonyl group, 4-isobenzofuranylcarbonyl group, 5-isobenzofuranylcarbonyl group, 2-benzothienylcarbonyl group, 3-benzothienylcarbonyl group, 4-benzothienylcarbonyl group, 5-benzothienylcarbonyl group, 6-benzothienylcarbonyl group, 7-benzothienylcarbonyl group, 1-isobenzothienylcarbonyl group, 4-isobenzothienylcarbonyl group, 5-isobenzothienylcarbonyl group, 2-chromenylcarbonyl group, 3-chromenylcarbonyl group, 4-chromenylcarbonyl group, 5-chromenylcarbonyl group, 6-chromenylcarbonyl group, 7-chromenylcarbonyl group, 8-chromenylcarbonyl group, 1-indolizinylcarbonyl group, 2-indolizinylcarbonyl group, 3-indolizinylcarbonyl group, 5-indolizinylcarbonyl group, 6-indolizinylcarbonyl group, 7-indolizinylcarbonyl group, 8-indolizinylcarbonyl group, 1-isoindolylcarbonyl group, 2-isoindolylcarbonyl group, 4-isoindolylcarbonyl group, 5-isoindolylcarbonyl group, 1-indolylcarbonyl group, 2-indolylcarbonyl group, 3-indolylcarbonyl group, 4-indolylcarbonyl group, 5-indolylcarbonyl group, 6-indolylcarbonyl group, 7-indolylcarbonyl group, 1-indazolylcarbonyl group, 2-indazolylcarbonyl group, 3-indazolylcarbonyl group, 4-indazolylcarbonyl group, 5-indazolylcarbonyl group, 6-indazolylcarbonyl group, 7-indazolylcarbonyl group, 1-purinylcarbonyl group, 2-purinylcarbonyl group, 3-purinylcarbonyl group, 6-purinylcarbonyl group, 7-purinylcarbonyl group, 8-purinylcarbonyl group, 2-quinolylcarbonyl group, 3-quinolylcarbonyl group, 4-quinolylcarbonyl group, 5-quinolylcarbonyl group, 6-quinolylcarbonyl group, 7-quinolylcarbonyl group, 8-quinolylcarbonyl group, 1-isoquinolylcarbonyl group, 3-isoquinolylcarbonyl group, 4-isoquinolylcarbonyl group, 5-isoquinolylcarbonyl group, 6-isoquinolylcarbonyl group, 7-isoquinolylcarbonyl group, 8-isoquinolylcarbonyl group, 1-phthalazinylcarbonyl group, 5-phthalazinylcarbonyl group, 6-phthalazinylcarbonyl group, 1-2,7-naphthyridinylcarbonyl group, 3-2,7-naphthyridinylcarbonyl group, 4-2,7-naphthyridinylcarbonyl group, 1-2,6-naphthyridinylcarbonyl group, 3-2,6-naphthyridinylcarbonyl group, 4-2,6-naphthyridinylcarbonyl group, 2-1,8-naphthyridinylcarbonyl group, 3-1,8-naphthyridinylcarbonyl group, 4-1,8-naphthyridinylcarbonyl group, 2-1,7-naphthyridinylcarbonyl group, 3-1,7-naphthyridinylcarbonyl group, 4-1,7-naphthyridinylcarbonyl group, 5-1,7-naphthyridinylcarbonyl group, 6-1,7-naphthyridinylcarbonyl group, 8-1,7-naphthyridinylcarbonyl group, 2-1,6-naphthyridinylcarbonyl group, 3-1,6-naphthyridinylcarbonyl group, 4-1,6-naphthyridinylcarbonyl group,

5-1,6-naphthyridinylcarbonyl group, 7-1,6-naphthyridinylcarbonyl group, 8-1,6-naphthyridinylcarbonyl group, 2-1,5-naphthyridinylcarbonyl group, 3-1,5-naphthyridinylcarbonyl group, 4-1,5-naphthyridinylcarbonyl group, 6-1,5-naphthyridinylcarbonyl group, 7-1,5-naphthyridinylcarbonyl group, 8-1,5-naphthyridinylcarbonyl group, 2-quinoxalinylcarbonyl group, 5-quinoxalinylcarbonyl group, 6-quinoxalinylcarbonyl group, 2-quinazolinylcarbonyl group, 4-quinazolinylcarbonyl group, 5-quinazolinylcarbonyl group, 6-quinazolinylcarbonyl group, 7-quinazolinylcarbonyl group, 8-quinazolinylcarbonyl group, 3-cinnolinylcarbonyl group, 4-cinnolinylcarbonyl group, 5-cinnolinylcarbonyl group, 6-cinnolinylcarbonyl group, 7-cinnolinylcarbonyl group, 8-cinnolinylcarbonyl group, 2-pteridinylcarbonyl group, 4-pteridinylcarbonyl group, 6-pteridinylcarbonyl group, 7-pteridinylcarbonyl group, and the like.

Preferably, 2-pyridylcarbonyl group, 3-pyridylcarbonyl group and 4-pyridylcarbonyl group may be mentioned.

Examples of C_{6-14} arylsulfonyl group are such as phenylsulfonyl, o-biphenylylsulfonyl, m-biphenylylsulfonyl, p-biphenylylsulfonyl, α-naphthylsulfonyl, β-naphthylsulfonyl, 1-anthrylsulfonyl, 2-anthrylsulfonyl, 9-anthrylsulfonyl, 1-phenanthrylsulfonyl, 2-phenanthrylsulfonyl, 3-phenanthrylsulfonyl, 4-phenanthrylsulfonyl, 9-phenanthrylsulfonyl and the like.

Preferably, phenylsulfonyl, o-biphenylylsulfonyl, m-biphenylylsulfonyl, p-biphenylylsulfonyl, α-naphthylsulfonyl and β-naphthylsulfonyl may be mentioned.

C_{2-9} heteroarylsulfonyl group includes C_{2-6} single-ring heterocyclic sulfonyl group with 5- to 7-member ring and C_{5-9} fused double-ring heterocyclic sulfonyl group with member atom number of 8 to 10, which may contain 1 to 3 hetero atoms selected from the group consisting of oxygen atom, nitrogen atom and sulfur atom alone or in a combination.

Examples of the C_{2-6} single-ring heterocyclic sulfonyl group with 5- to 7-member ring are such as 2-thienylsulfonyl group, 3-thienylsulfonyl group, 2-furylsulfonyl group, 3-furylsulfonyl group, 2-pyranylsulfonyl group, 3-pyranylsulfonyl group, 4-pyranylsulfonyl group, 1-pyrrolylsulfonyl group, 2-pyrrolylsulfonyl group, 3-pyrrolylsulfonyl group, 1-imidazolylsulfonyl group, 2-imidazolylsulfonyl group, 4-imidazolylsulfonyl group, 1-pyrazolylsulfonyl group, 3-pyrazolylsulfonyl group, 4-pyrazolylsulfonyl group, 2-thiazolylsulfonyl group, 4-thiazolylsulfonyl group, 5-thiazolylsulfonyl group, 3-isothiazolylsulfonyl group, 4-isothiazolylsulfonyl group, 5-isothiazolylsulfonyl group, 2-oxazolylsulfonyl group, 4-oxazolylsulfonyl group,

5-oxazolylsulfonyl group, 3-isoxazolylsulfonyl group, 4-isoxazolylsulfonyl group, 5-isoxazolylsulfonyl group, 2-pyridylsulfonyl group, 3-pyridylsulfonyl group, 4-pyridylsulfonyl group, 2-pyradinylsulfonyl group, 2-pyrimidinylsulfonyl group, 4-pyrimidinylsulfonyl group, 5-pyrimidinylsulfonyl group, 3-pyridazinylsulfonyl group, 4-pyridazinylsulfonyl group, 2-1,3,4-oxadiazolylsulfonyl group, 2-1,3,4-thiadiazolylsulfonyl group, 3-1,2,4-oxadiazolylsulfonyl group, 5-1,2,4-oxadiazolylsulfonyl group, 3-1,2,4-thiadiazolylsulfonyl group, 5-1,2,4-thiadiazolylsulfonyl group, 3-1,2,5-oxadiazolylsulfonyl group, 3-1,2,5-thiadiazolylsulfonyl group and the like.

Examples of the C_{5-9} fused double-ring heterocyclic sulfonyl group with member atom number of 8 to 10 are 2-benzofuranylsulfonyl group, 3-benzofuranylsulfonyl group, 4-benzofuranylsulfonyl group, 5-benzofuranylsulfonyl group, 6-benzofuranylsulfonyl group, 7-benzofuranylsulfonyl group, 1-isobenzofuranylsulfonyl group, 4-isobenzofuranylsulfonyl group, 5-isobenzofuranylsulfonyl group, 2-benzothienylsulfonyl group, 3-benzothienylsulfonyl group, 4-benzothienylsulfonyl group, 5-benzothienylsulfonyl group, 6-benzothienylsulfonyl group, 7-benzothienylsulfonyl group, 1-isobenzothienylsulfonyl group, 4-isobenzothienylsulfonyl group, 5-isobenzothienylsulfonyl group, 2-chromenylsulfonyl group, 3-chromenylsulfonyl group, 4-chromenylsulfonyl group, 5-chromenylsulfonyl group, 6-chromenylsulfonyl group, 7-chromenylsulfonyl group, 8-chromenylsulfonyl group, 1-indolizinylsulfonyl group, 2-indolizinylsulfonyl group, 3-indolizinylsulfonyl group, 5-indolizinylsulfonyl group, 6-indolizinylsulfonyl group, 7-indolizinylsulfonyl group, 8-indolizinylsulfonyl group, 1-isoindolylsulfonyl group, 2-isoindolylsulfonyl group, 4-isoindolylsulfonyl group, 5-isoindolylsulfonyl group, 1-indolylsulfonyl group, 2-indolylsulfonyl group, 3-indolylsulfonyl group, 4-indolylsulfonyl group, 5-indolylsulfonyl group, 6-indolylsulfonyl group, 7-indolylsulfonyl group, 1-indazolylsulfonyl group, 2-indazolylsulfonyl group, 3-indazolylsulfonyl group, 4-indazolylsulfonyl group, 5-indazolylsulfonyl group, 6-indazolylsulfonyl group, 7-indazolylsulfonyl group, 1-purinylsulfonyl group, 2-purinylsulfonyl group, 3-purinylsulfonyl group, 6-purinylsulfonyl group, 7-purinylsulfonyl group, 8-purinylsulfonyl group, 2-quinolylsulfonyl group, 3-quinolylsulfonyl group, 4-quinolylsulfonyl group, 5-quinolylsulfonyl group, 6-quinolylsulfonyl group, 7-quinolylsulfonyl group, 8-quinolylsulfonyl group, 1-isoquinolylsulfonyl group, 3-isoquinolylsulfonyl group, 4-isoquinolylsulfonyl group, 5-isoquinolylsulfonyl group, 6-isoquinolylsulfonyl group, 7-isoquinolylsulfonyl group,

8-isoquinolylsulfonyl group, 1-phthalazinylsulfonyl group, 5-phthalazinylsulfonyl group, 6-phthalazinylsulfonyl group, 1-2,7-naphthyridinylsulfonyl group, 3-2,7-naphthyridinylsulfonyl group, 4-2,7-naphthyridinylsulfonyl group, 1-2,6-naphthyridinylsulfonyl group, 3-2,6-naphthyridinylsulfonyl group, 4-2,6-naphthyridinylsulfonyl group, 2-1,8-naphthyridinylsulfonyl group, 3-1,8-naphthyridinylsulfonyl group, 4-1,8-naphthyridinylsulfonyl group, 2-1,7-naphthyridinylsulfonyl group, 3-1,7-naphthyridinylsulfonyl group, 4-1,7-naphthyridinylsulfonyl group, 5-1,7-naphthyridinylsulfonyl group, 6-1,7-naphthyridinylsulfonyl group, 8-1,7-naphthyridinylsulfonyl group, 2-1,6-naphthyridinylsulfonyl group, 3-1,6-naphthyridinylsulfonyl group, 4-1,6-naphthyridinylsulfonyl group, 5-1,6-naphthyridinylsulfonyl group, 7-1,6-naphthyridinylsulfonyl group, 8-1,6-naphthyridinylsulfonyl group, 2-1,5-naphthyridinylsulfonyl group, 3-1,5-naphthyridinylsulfonyl group, 4-1,5-naphthyridinylsulfonyl group, 6-1,5-naphthyridinylsulfonyl group, 7-1,5-naphthyridinylsulfonyl group, 8-1,5-naphthyridinylsulfonyl group, 2-quinoxalinylsulfonyl group, 5-quinoxalinylsulfonyl group, 6-quinoxalinylsulfonyl group, 2-quinazolinylsulfonyl group, 4-quinazolinylsulfonyl group, 5-quinazolinylsulfonyl group, 6-quinazolinylsulfonyl group, 7-quinazolinylsulfonyl group, 8-quinazolinylsulfonyl group, 3-cinnolinylsulfonyl group, 4-cinnolinylsulfonyl group, 5-cinnolinylsulfonyl group, 6-cinnolinylsulfonyl group, 7-cinnolinylsulfonyl group, 8-cinnolinylsulfonyl group, 2-pteridinylsulfonyl group, 4-pteridinylsulfonyl group, 6-pteridinylsulfonyl group, 7-pteridinylsulfonyl group, and the like.

Preferably, 2-pyridylsulfonyl group, 3-pyridylsulfonyl group and 4-pyridylsulfonyl group may be mentioned.

Examples of C_{6-14} arylamino group are such as phenylamino, o-biphenylylamino, m-biphenylylamino, p-biphenylylamino, α-naphthylamino, β-naphthylamino, 1-anthrylamino, 2-anthrylamino, 9-anthrylamino, 1-phenanthrylamino, 2-phenanthrylamino, 3-phenanthrylamino, 4-phenanthrylamino, 9-phenanthrylamino and the like.

Preferably, phenylamino, o-biphenylylamino, m-biphenylylamino, p-biphenylylamino, α-naphthylamino and β-naphthylamino may be mentioned.

C_{2-9} heteroarylamino group includes C_{2-6} single-ring heterocyclic amino group with 5- to 7-member ring and C_{5-9} fused double-ring heterocyclic amino group with member atom number of 8 to 10, which may contain 1 to 3 hetero atoms selected from the group consisting of oxygen atom, nitrogen atom and sulfur atom alone or in a

combination.

Examples of the C_{2-6} single-ring heterocyclic amino group with 5- to 7-member ring are such as 2-thienylamino group, 3-thienylamino group, 2-furylamino group, 3-furylamino group, 2-pyranylamino group, 3-pyranylamino group, 4-pyranylamino group, 1-pyrrolylamino group, 2-pyrrolylamino group, 3-pyrrolylamino group, 1-imidazolylamino group, 2-imidazolylamino group, 4-imidazolylamino group, 1-pyrazolylamino group, 3-pyrazolylamino group, 4-pyrazolylamino group, 2-thiazolylamino group, 4-thiazolylamino group, 5-thiazolylamino group, 3-isothiazolylamino group, 4-isothiazolylamino group, 5-isothiazolylamino group, 2-oxazolylamino group, 4-oxazolylamino group, 5-oxazolylamino group, 3-isoxazolylamino group, 4-isoxazolylamino group, 5-isoxazolylamino group, 2-pyridylamino group, 3-pyridylamino group, 4-pyridylamino group, 2-pyradinylamino group, 2-pyrimidinylamino group, 4-pyrimidinylamino group, 5-pyrimidinylamino group, 3-pyridazinylamino group, 4-pyridazinylamino group, 2-1,3,4-oxadiazolylamino group, 2-1,3,4-thiadiazolylamino group, 3-1,2,4-oxadiazolylamino group, 5-1,2,4-oxadiazolylamino group, 3-1,2,4-thiadiazolylamino group, 5-1,2,4-thiadiazolylamino group, 3-1,2,5-oxadiazolylamino group, 3-1,2,5-thiadiazolylamino group and the like.

Examples of the C_{5-9} fused double-ring heterocyclic amino group with member atom number of 8 to 10 are 2-benzofuranylamino group, 3-benzofuranylamino group, 4-benzofuranylamino group, 5-benzofuranylamino group, 6-benzofuranylamino group, 7-benzofuranylamino group, 1-isobenzofuranylamino group, 4-isobenzofuranylamino group, 5-isobenzofuranylamino group, 2-benzothienylamino group, 3-benzothienylamino group, 4-benzothienylamino group, 5-benzothienylamino group, 6-benzothienylamino group, 7-benzothienylamino group, 1-isobenzothienylamino group, 4-isobenzothienylamino group, 5-isobenzothienylamino group, 2-chromenylamino group, 3-chromenylamino group, 4-chromenylamino group, 5-chromenylamino group, 6-chromenylamino group, 7-chromenylamino group, 8-chromenylamino group, 1-indolizinylamino group, 2-indolizinylamino group, 3-indolizinylamino group, 5-indolizinylamino group, 6-indolizinylamino group, 7-indolizinylamino group, 8-indolizinylamino group, 1-isoindolylamino group, 2-isoindolylamino group, 4-isoindolylamino group, 5-isoindolylamino group, 1-indolylamino group, 2-indolylamino group, 3-indolylamino group, 4-indolylamino group, 5-indolylamino group, 6-indolylamino group, 7-indolylamino group, 1-indazolylamino group, 2-indazolylamino group,

3-indazolylamino group, 4-indazolylamino group, 5-indazolylamino group, 6-indazolylamino group, 7-indazolylamino group, 1-purinylamino group, 2-purinylamino group, 3-purinylamino group, 6-purinylamino group, 7-purinylamino group, 8-purinylamino group, 2-quinolylamino group, 3-quinolylamino group, 4-quinolylamino group, 5-quinolylamino group, 6-quinolylamino group, 7-quinolylamino group, 8-quinolylamino group, 1-isoquinolylamino group, 3-isoquinolylamino group, 4-isoquinolylamino group, 5-isoquinolylamino group, 6-isoquinolylamino group, 7-isoquinolylamino group, 8-isoquinolylamino group, 1-phthalazinylamino group, 5-phthalazinylamino group, 6-phthalazinylamino group, 1-2,7-naphthyridinylamino group, 3-2,7-naphthyridinylamino group, 4-2,7-naphthyridinylamino group, 1-2,6-naphthyridinylamino group, 3-2,6-naphthyridinylamino group, 4-2,6-naphthyridinylamino group, 2-1,8-naphthyridinylamino group, 3-1,8-naphthyridinylamino group, 4-1,8-naphthyridinylamino group, 2-1,7-naphthyridinylamino group, 3-1,7-naphthyridinylamino group, 4-1,7-naphthyridinylamino group, 5-1,7-naphthyridinylamino group, 6-1,7-naphthyridinylamino group, 8-1,7-naphthyridinylamino group, 2-1,6-naphthyridinylamino group, 3-1,6-naphthyridinylamino group, 4-1,6-naphthyridinylamino group, 5-1,6-naphthyridinylamino group, 7-1,6-naphthyridinylamino group, 8-1,6-naphthyridinylamino group, 2-1,5-naphthyridinylamino group, 3-1,5-naphthyridinylamino group, 4-1,5-naphthyridinylamino group, 6-1,5-naphthyridinylamino group, 7-1,5-naphthyridinylamino group, 8-1,5-naphthyridinylamino group, 2-quinoxalinylamino group, 5-quinoxalinylamino group, 6-quinoxalinylamino group, 2-quinazolinylamino group, 4-quinazolinylamino group, 5-quinazolinylamino group, 6-quinazolinylamino group, 7-quinazolinylamino group, 8-quinazolinylamino group, 3-cinnolinylamino group, 4-cinnolinylamino group, 5-cinnolinylamino group, 6-cinnolinylamino group, 7-cinnolinylamino group, 8-cinnolinylamino group, 2-pteridinylamino group, 4-pteridinylamino group, 6-pteridinylamino group, 7-pteridinylamino group, and the like.

Preferably, 2-pyridylamino group, 3-pyridylamino group and 4-pyridylamino group may be mentioned.

Concrete examples of substituents on the compounds used in the present invention are as follows.

Concrete examples of R^1 and R^2 are preferably methyl.

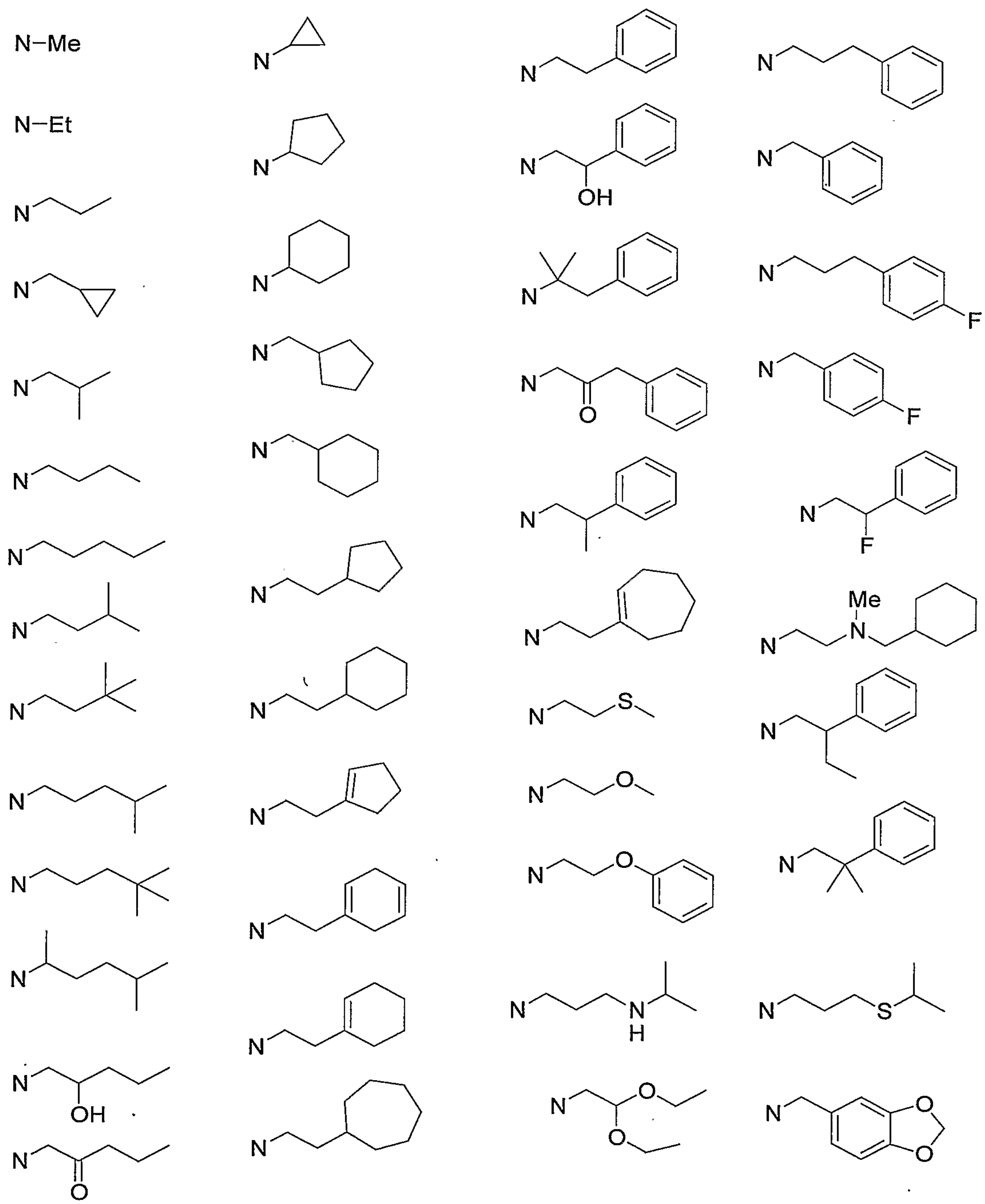
Concrete examples of R^3 are preferably hydroxy group.

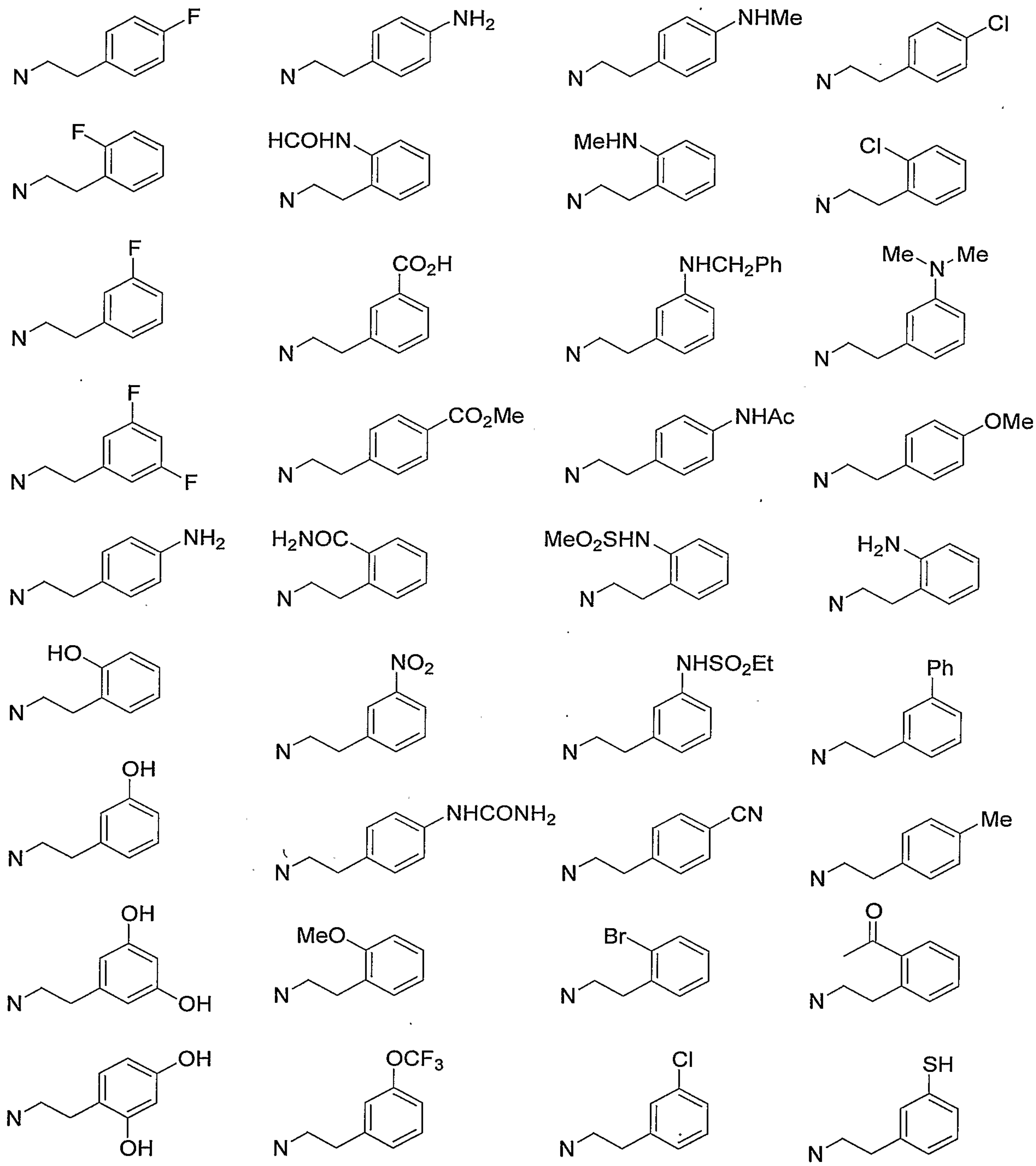
Concrete examples of R^4 are preferably hydrogen atom.

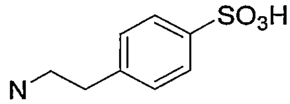
Concrete examples of R^5 are preferably hydrogen atom.

Concrete examples of $-N-(CH_2)_m-V-(CH_2)_n-R^6$ are preferably the following 1) to 4).

1)



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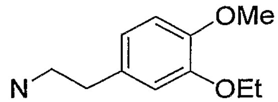
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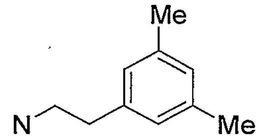
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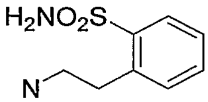
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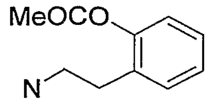
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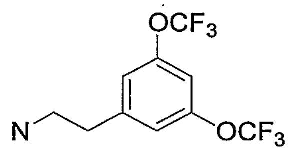
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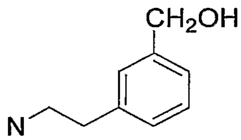
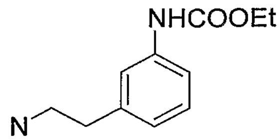
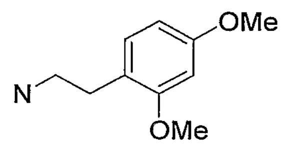
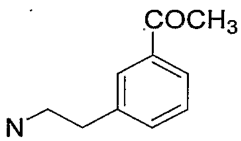
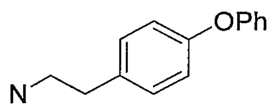

CH2OH
N


NHCOOEt
N


OMe
OMe
N


COCH3
N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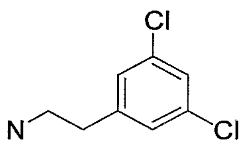
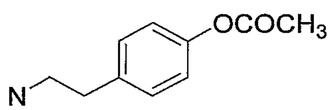
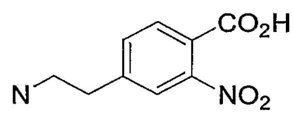
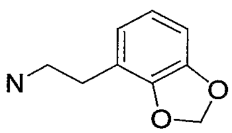
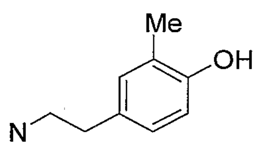
N

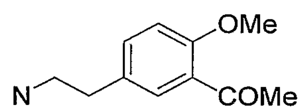

Cl
Cl
N

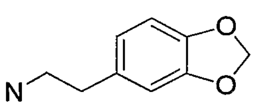

OCOCH3
N

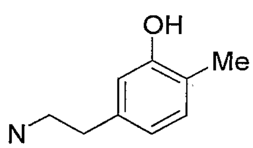

CO2H
NO2
N

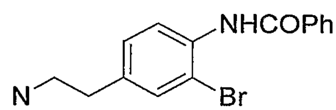

N
O
O

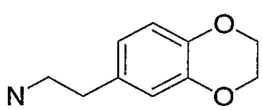

Me
OH
N

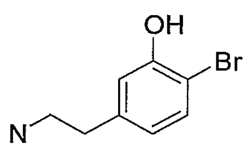

OMe
COMe
N

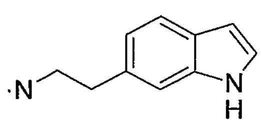

O
O
N

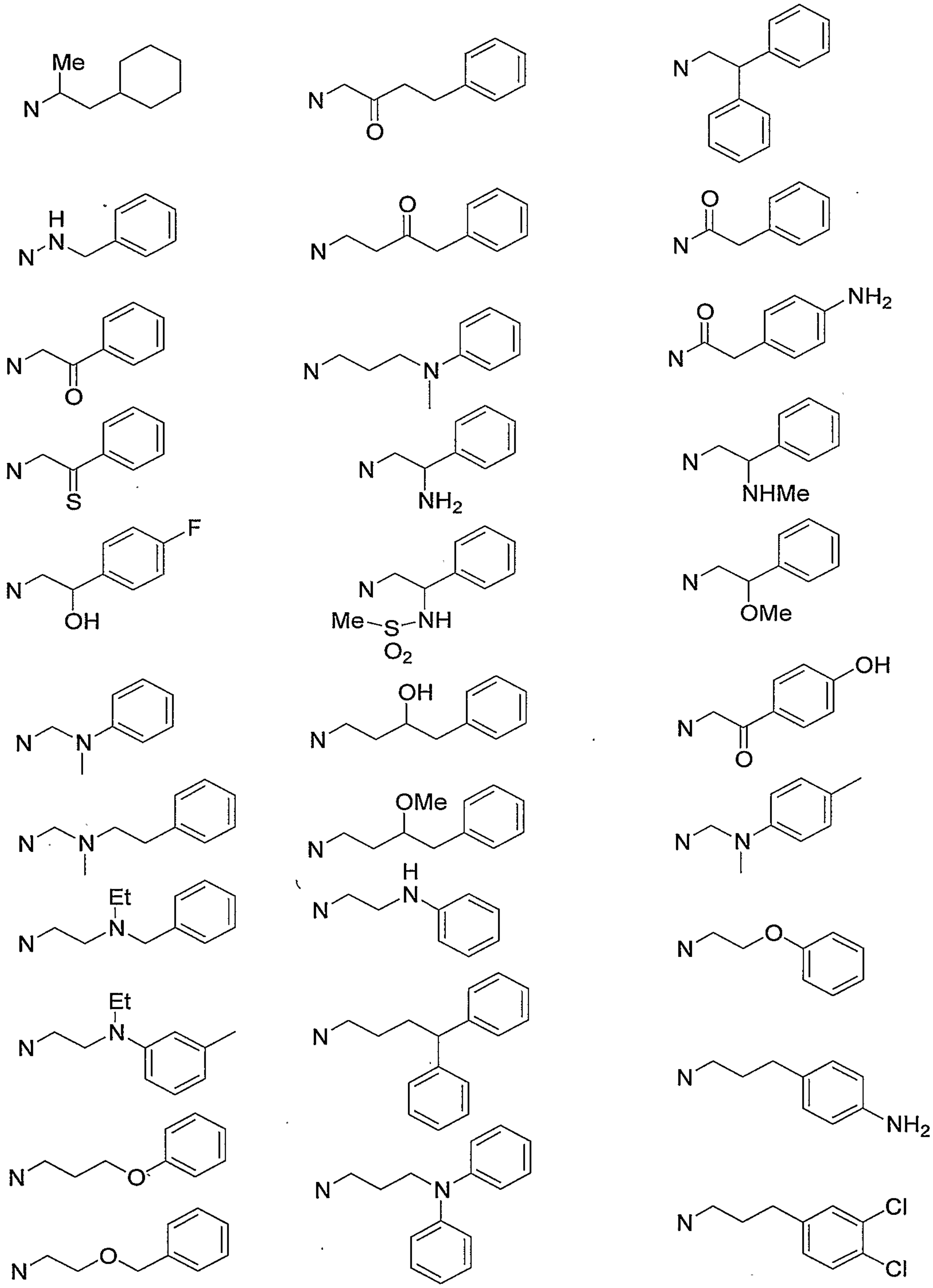

OH
Me
N

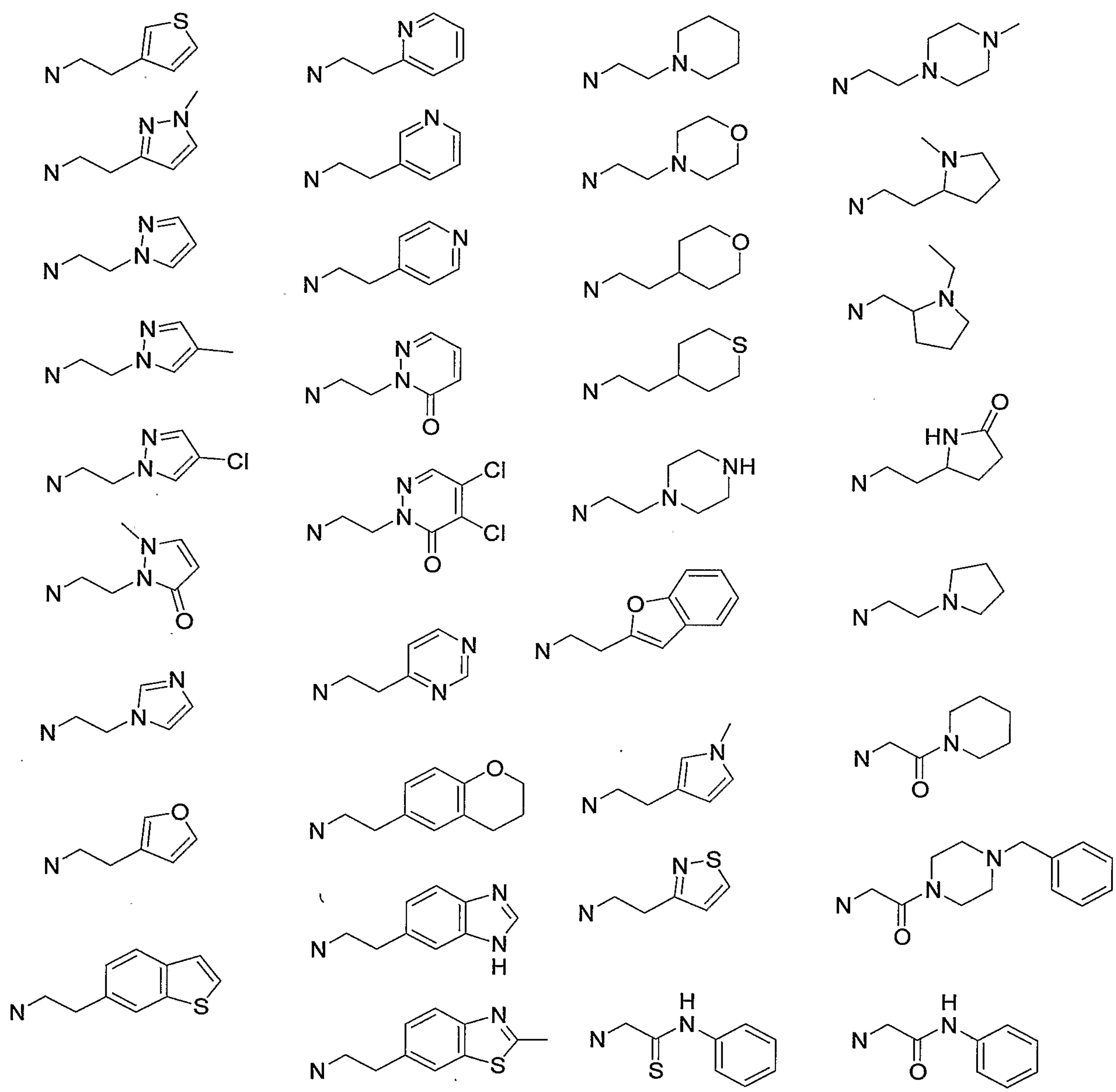

NHCOPh
Br
N


O
O
N


OH
Br
N


N
N
H





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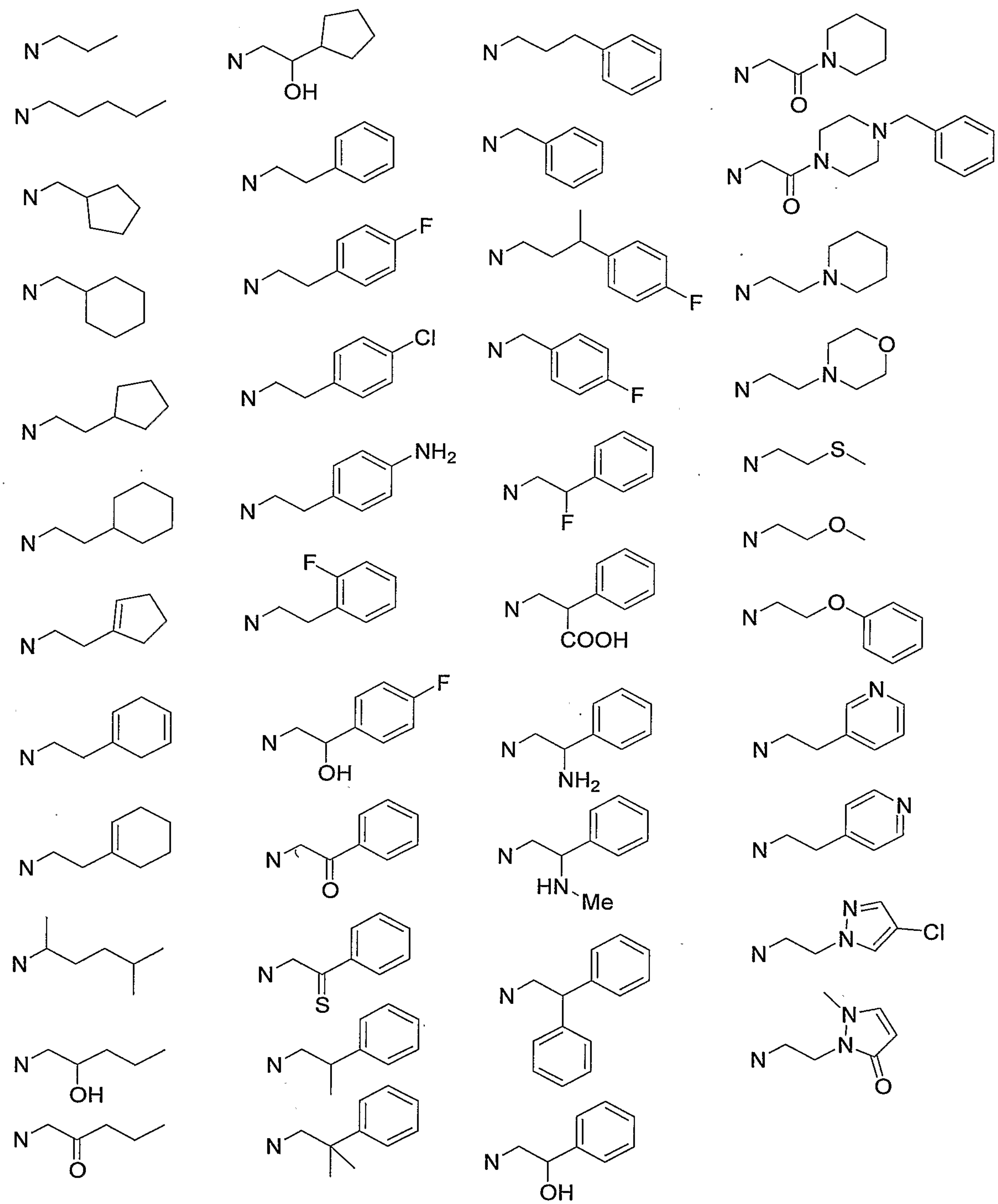

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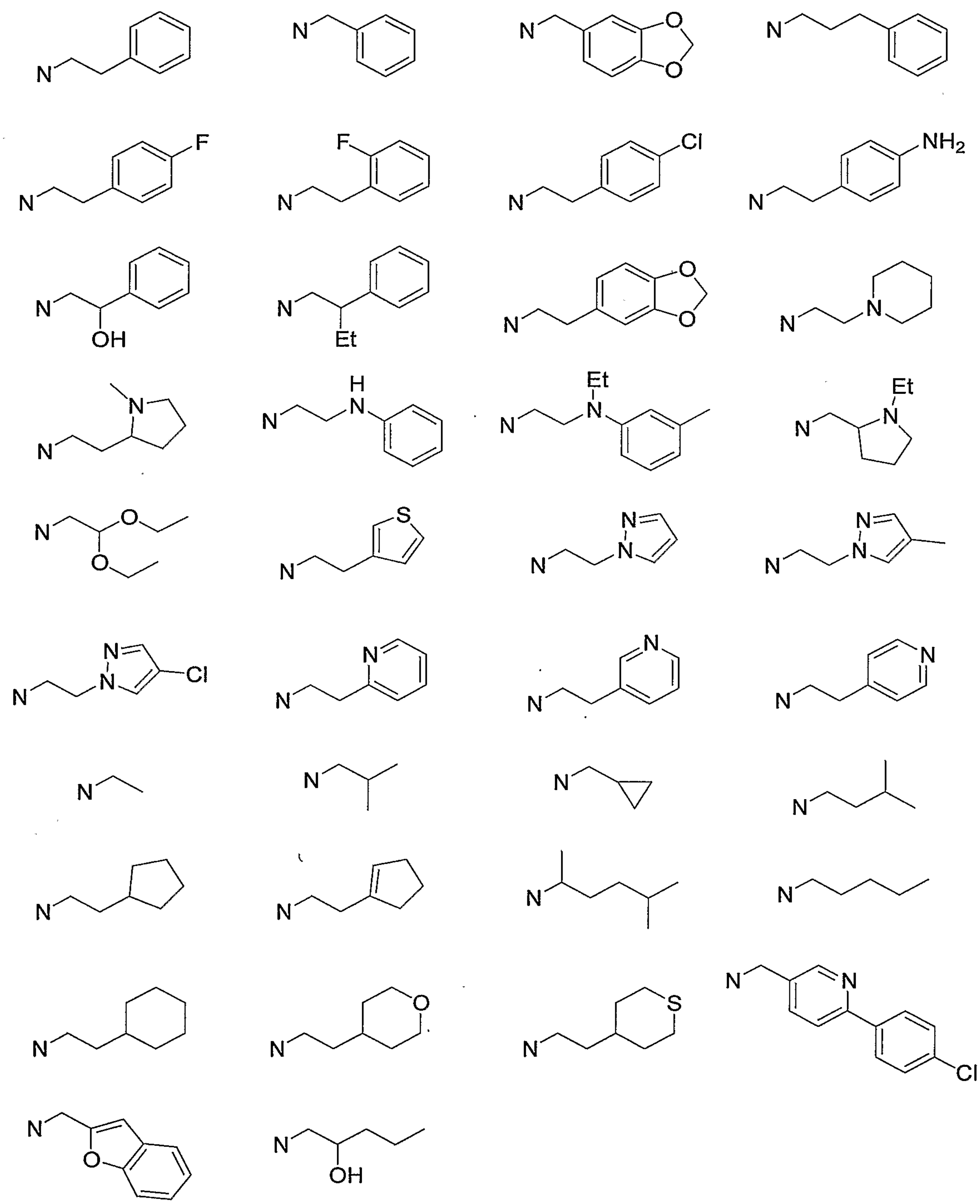

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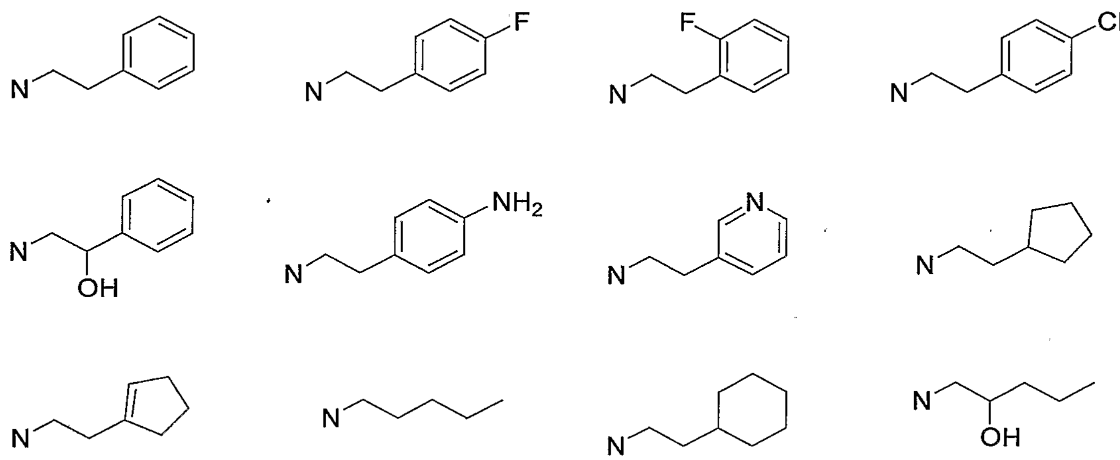
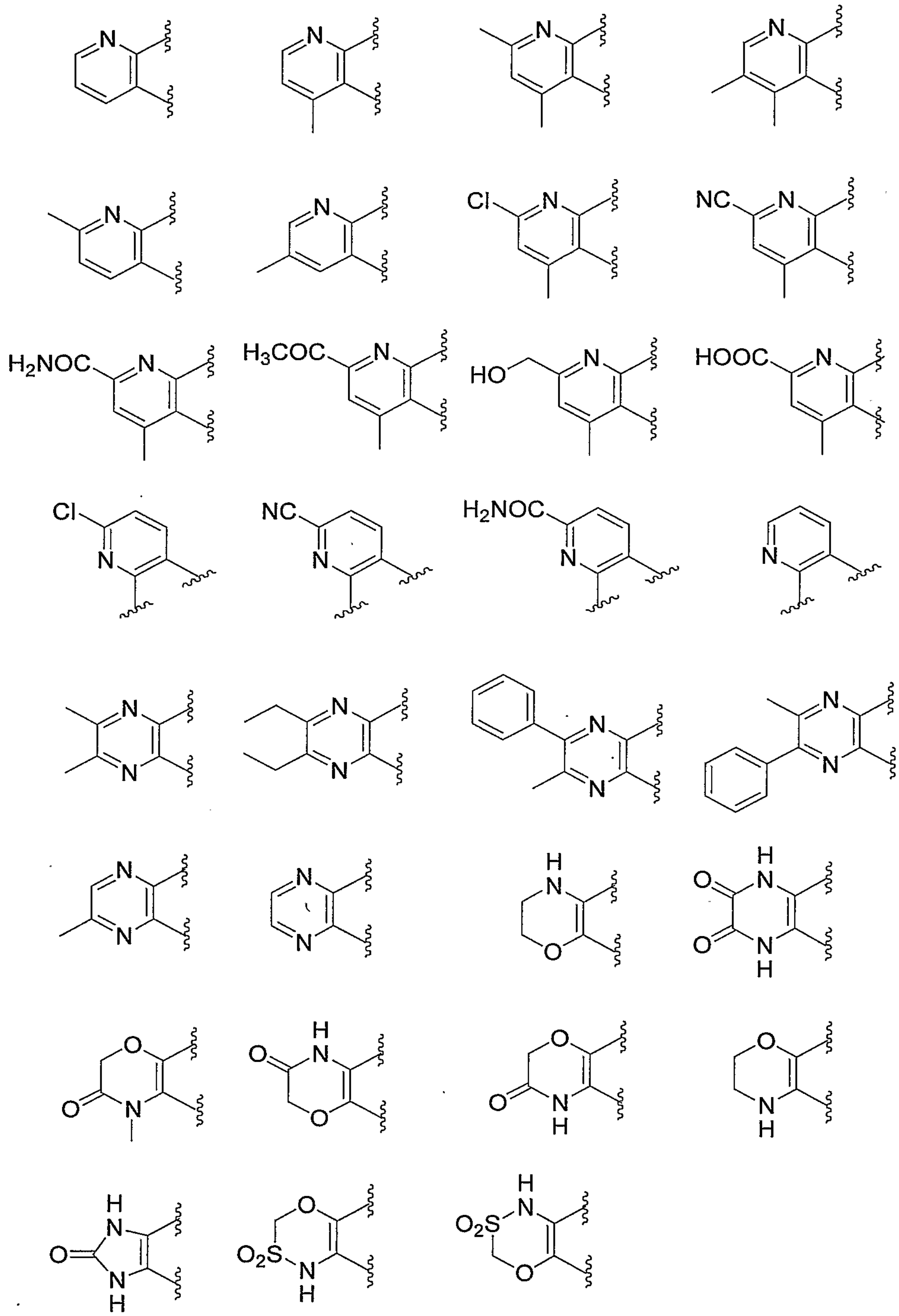


Concrete examples of A are preferably the following 1) and 2).


N
N
N
N
N
N
Cl
N
NC
N
H2NOC
N
H3COC
N
HO
N
HOOC
N
Cl
N
NC
N
H2NOC
N
N
N
N
N
N
N
N
N
N
N
N
N
N
H
N
O
O
H
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O
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O
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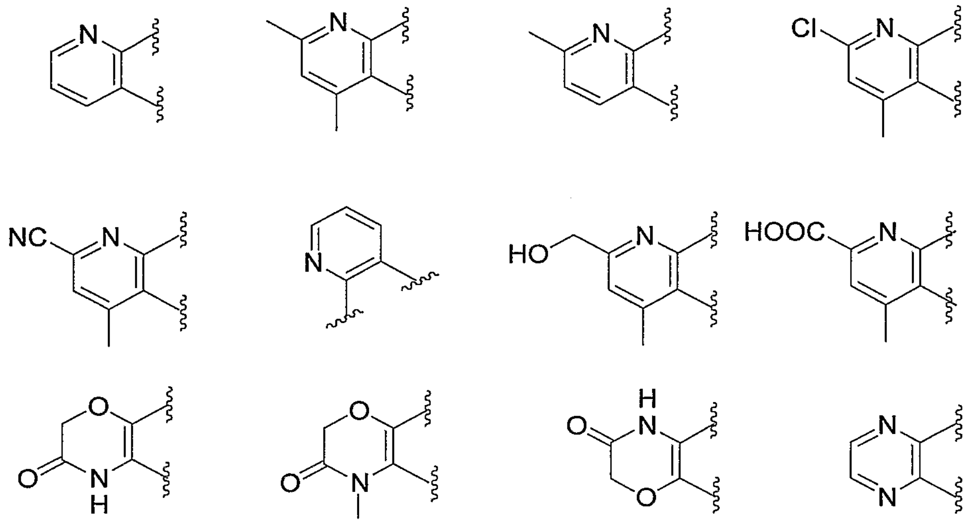
N
O2S
O

2)



The preferable compounds used in the present invention include the followings:

(1) A benzopyran derivative of formula (I) or (II), or pharmaceutically acceptable salt thereof, wherein both R^1 and R^2 are methyl, R^3 is hydroxy group, and R^4 is hydrogen atom;

(2) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (1), which is the compound of formula (I);

(3) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (2), wherein V is a bond, m is an integer of 1 to 3, n is 0 or 1 and R^6 is benzene ring;

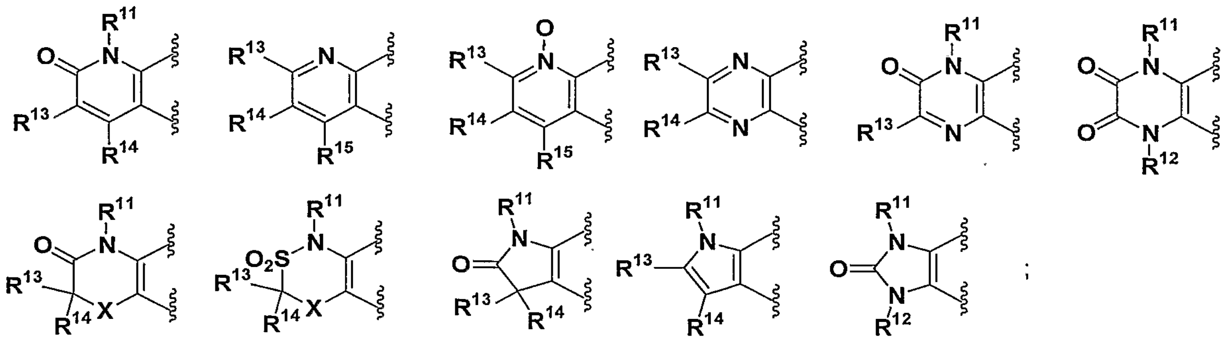
(4) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), wherein V is CR^7R^8 wherein R^7 is hydroxy group and R^8 is hydrogen atom, and m is 0 or 1;

(5) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), wherein R^6 is alkyl group, cycloalkyl group or cycloalkynyl ring;

(6) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein V is CR^7R^8 wherein R^7 is hydroxy group and R^8 is hydrogen atom, and m is 0 or 1;

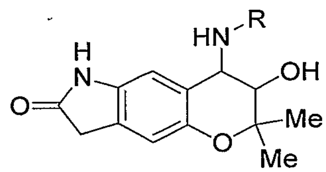
(7) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), wherein A is the group of formula (VIII)

Formula (VIII)

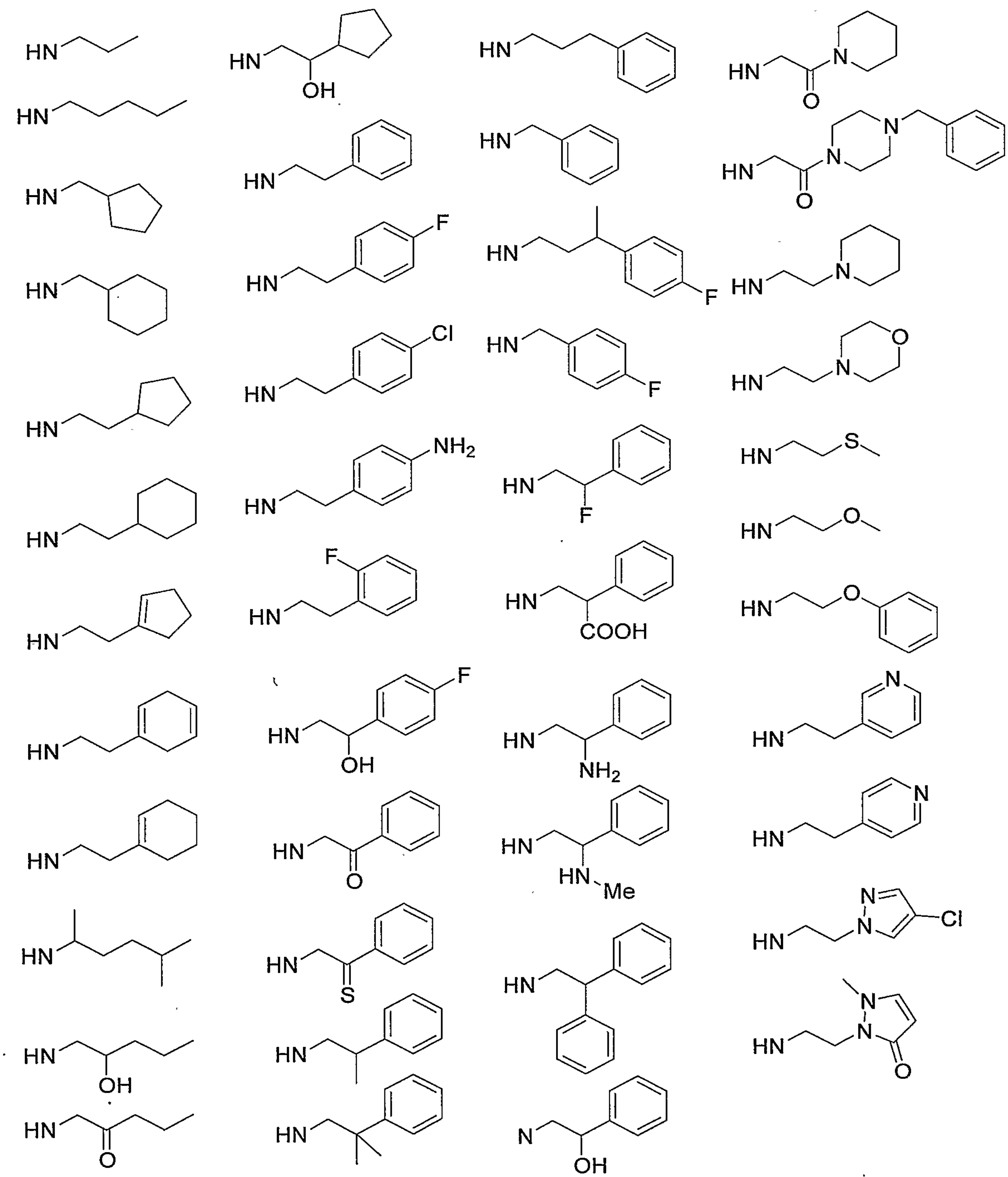


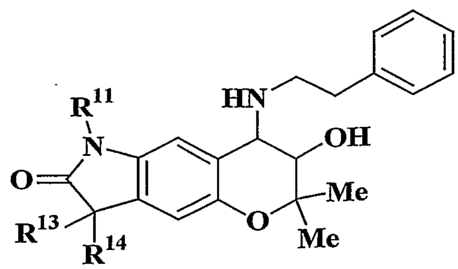
(8) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (4), wherein A is the group of formula (VIII);
(9) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein A is the group of formula (VIII);
(10) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (6), wherein A is the group of formula (VIII);

Hereinafter, concrete examples of the compounds that can be used in the present invention are shown, but the present invention is not limited thereto. In the meanwhile, "Me" means methyl, "Et" means ethyl, "Pr" means propyl, "Bu" means butyl, "Ac" means acetyl ($COCH_3$), and "-" means a bond.

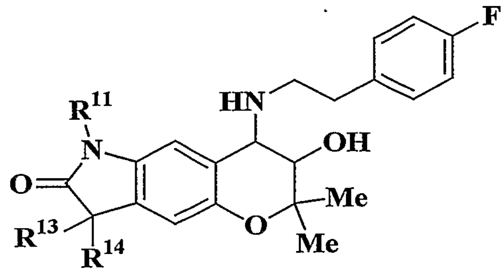


HN—R

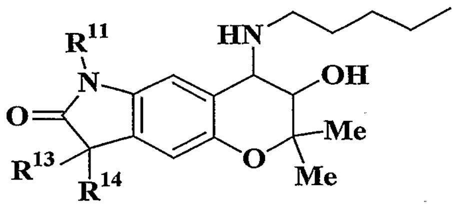




R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



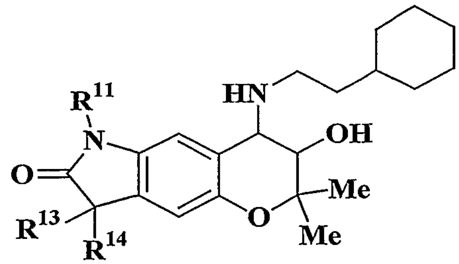
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	H	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

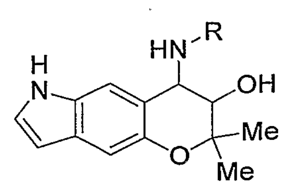
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	H	H
CH_2CH_2Ph	Ph	H



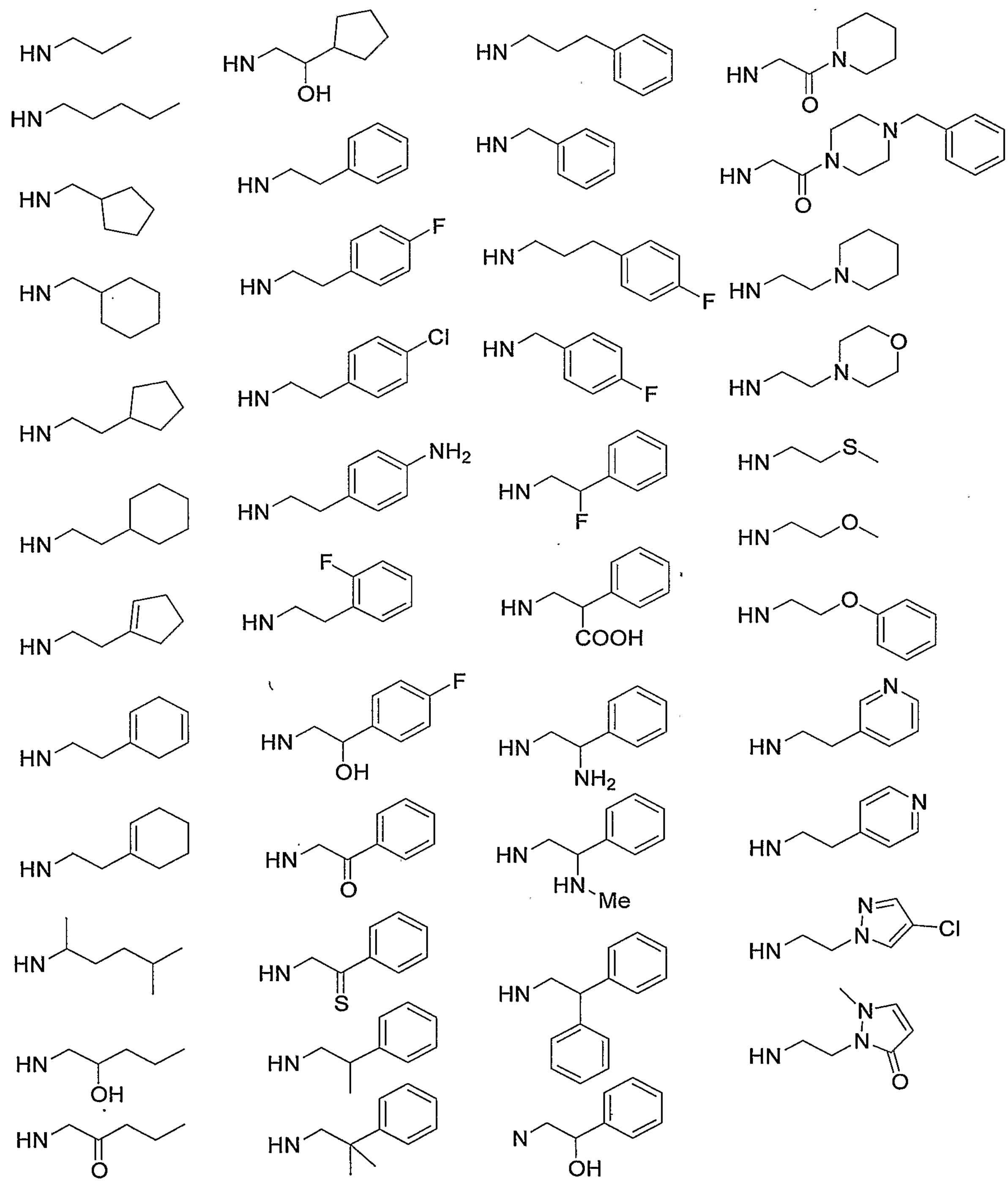
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

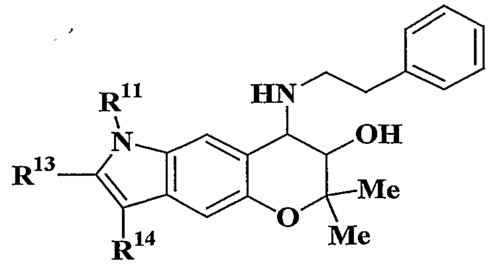
R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	H	H
CH_2CH_2Ph	Ph	H

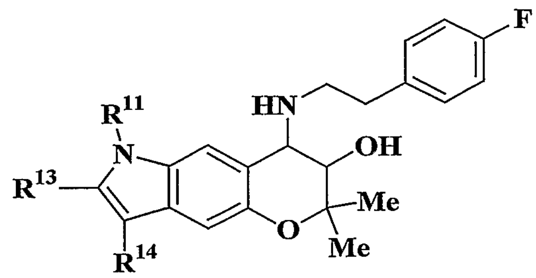


HN—R

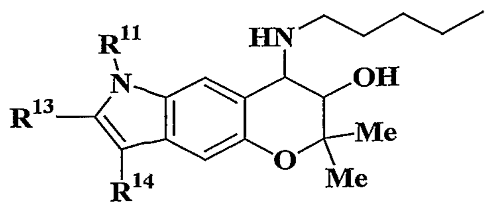




R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



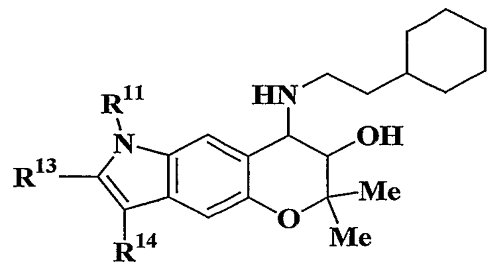
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



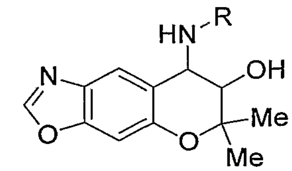
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

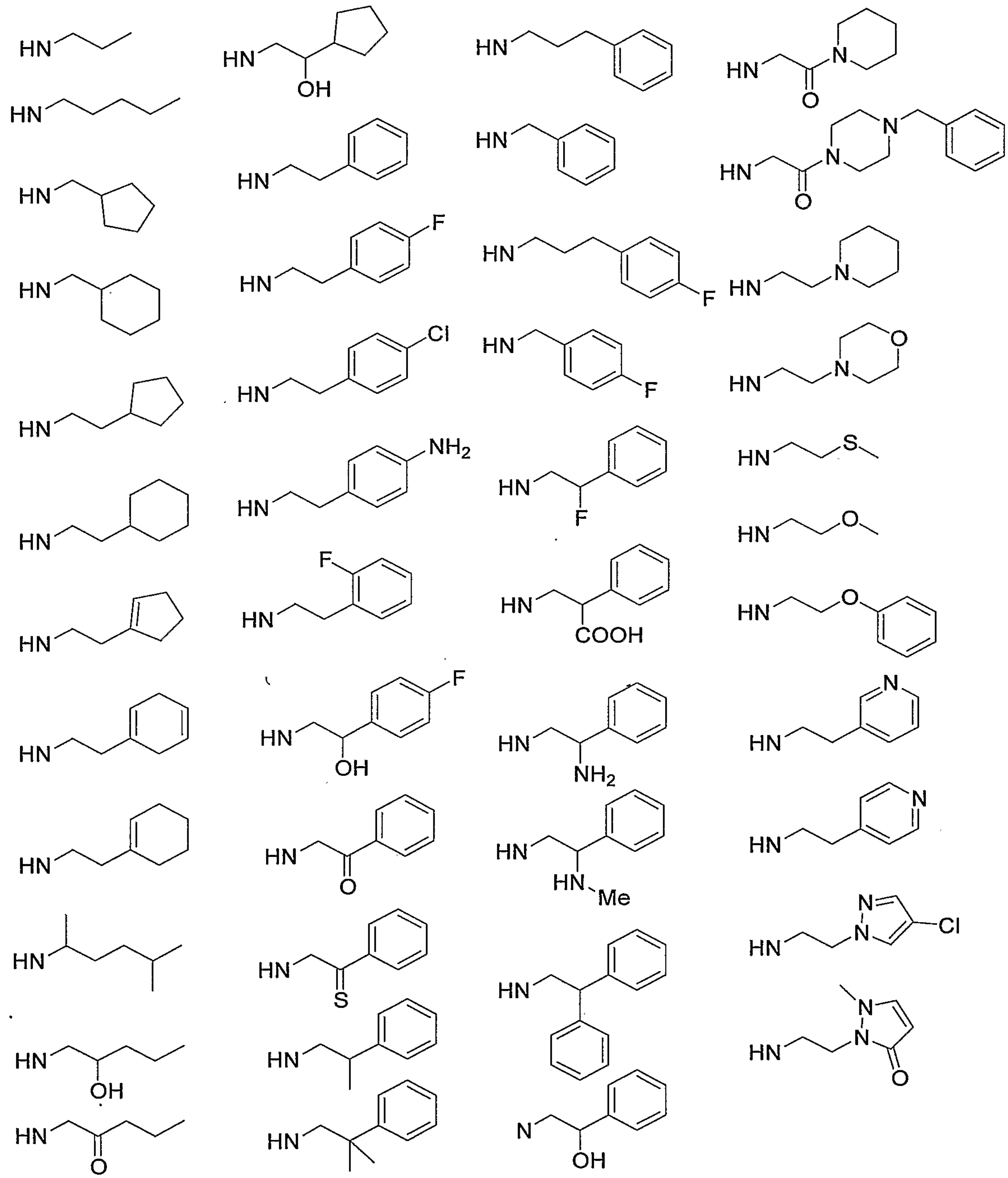
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H

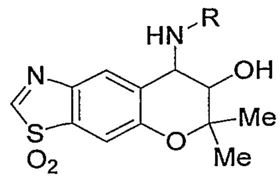


R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H

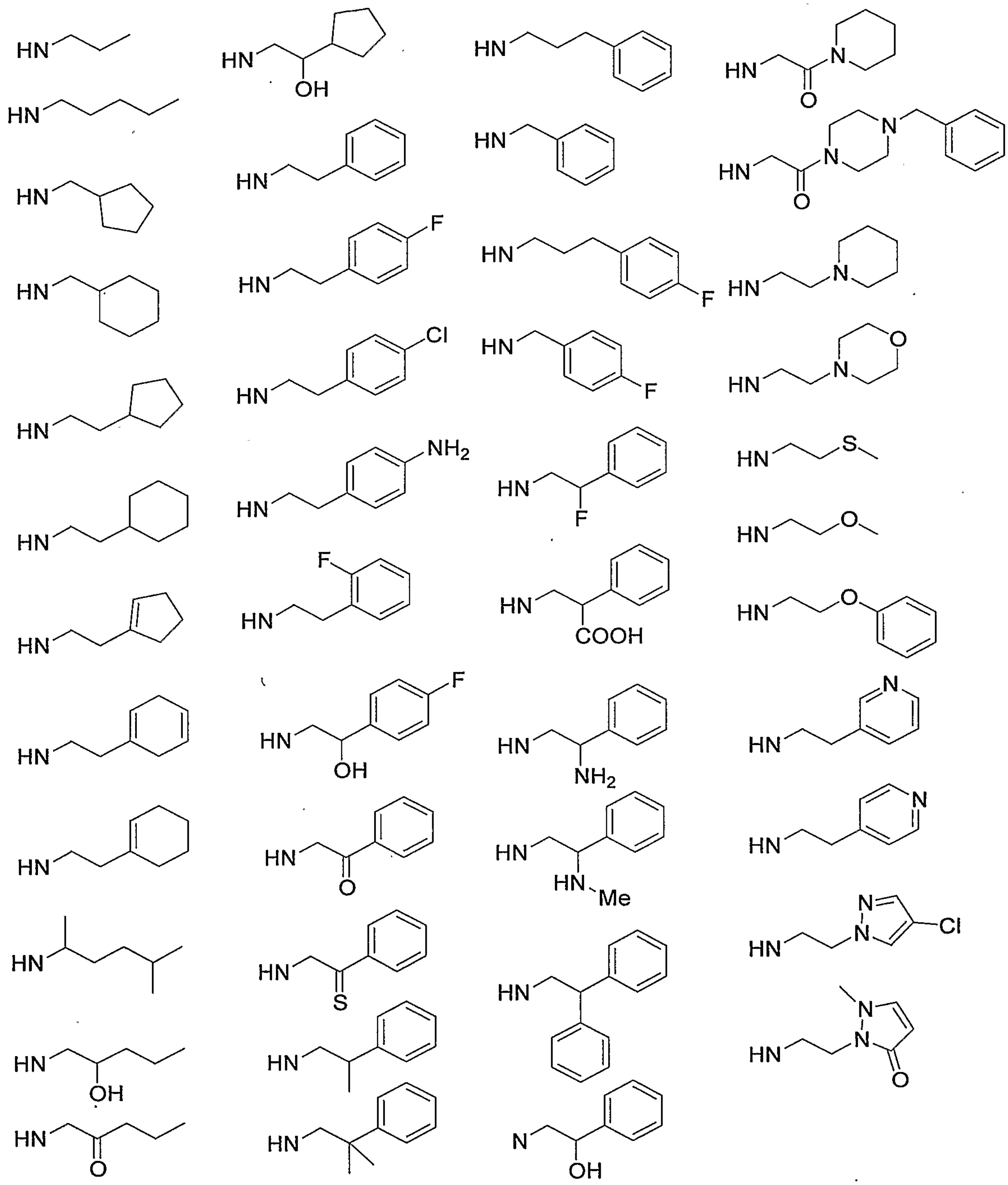


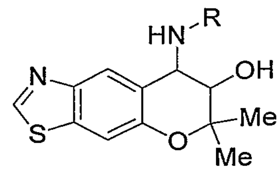
HN—R



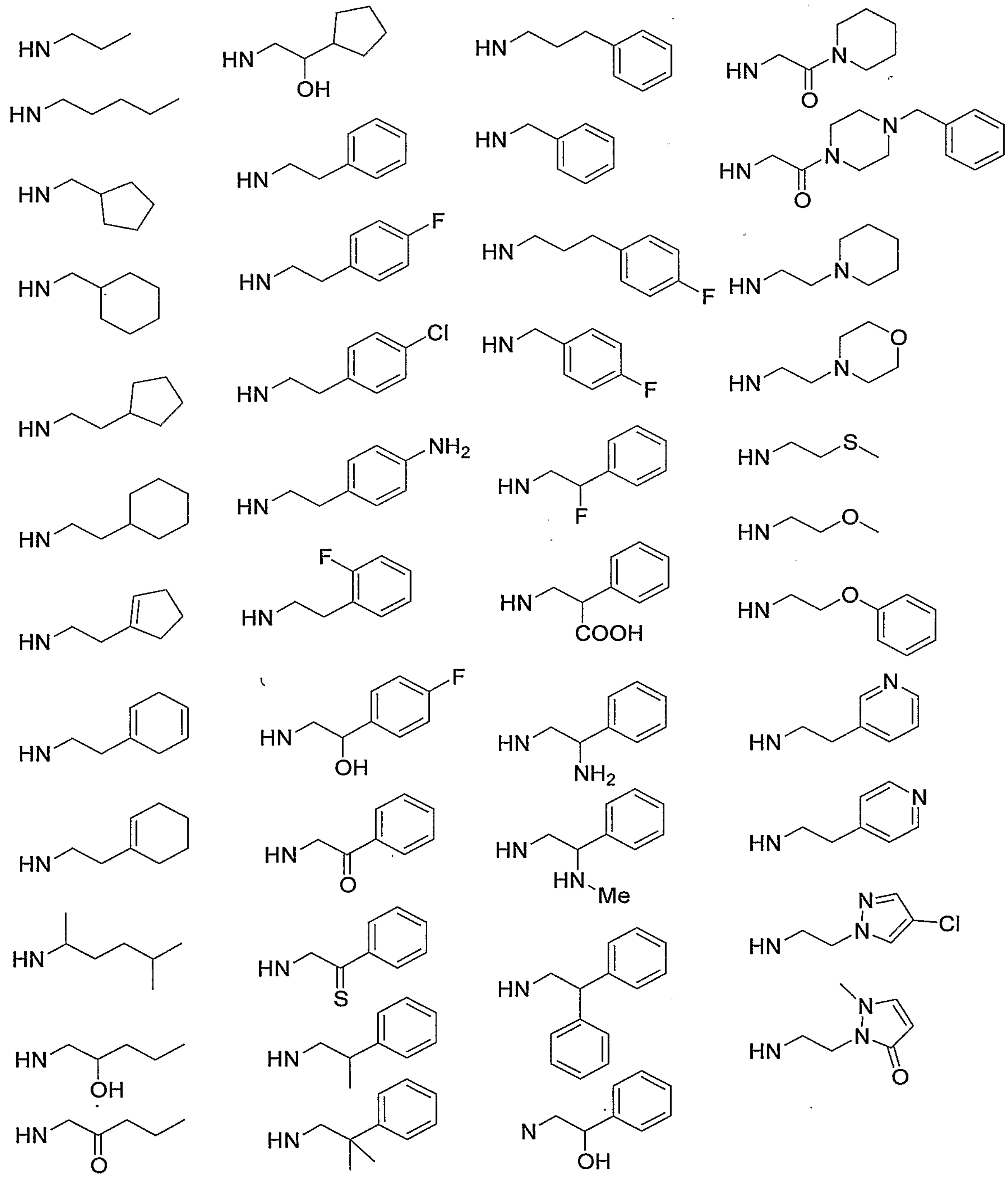


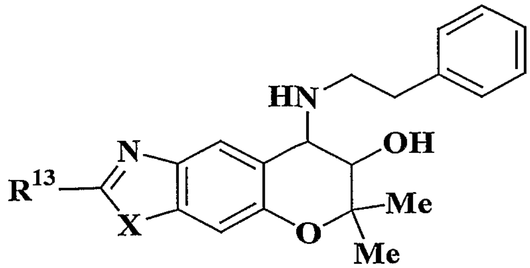
HN—R



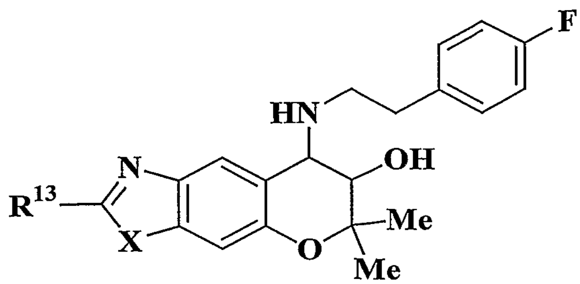


HN—R

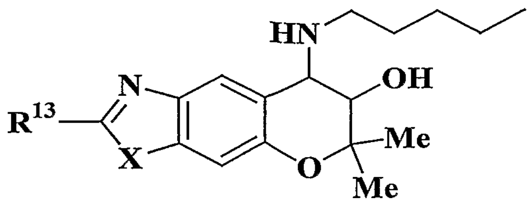




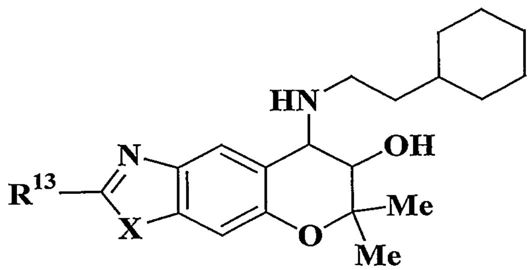
R^{13}	X	R^{13}	X
NO_2	O	Me	O
CHO	O	Et	O
SO_3H	O	iPr	O
Cl	O	nPr	O
Br	O	nBu	O
CH_2OH	O	tBu	O
CH_2NH_2	O	Ph	O
CH_2NHMe	O	CH_2Ph	O
CH_2Ph	SO	CH_2CH_2Ph	O
COMe	SO	Me	S
COOH	SO	Et	S
$CONH_2$	SO	iPr	S
CONHMe	SO	nPr	S
CONHMs	SO	nBu	S
NHMs	SO	tBu	S
NHCOMe	SO	Ph	S
NO_2	SO_2	CH_2Ph	S
CHO	S	CH_2CH_2Ph	S
SO_3H	S	Me	SO_2
SO_2NHMe	SO_2	Et	SO_2
OH	SO	iPr	SO_2
COMe	O	nPr	SO_2
COOH	O	nBu	SO_2
$CONH_2$	O	tBu	SO_2
CONHMe	O	Ph	SO_2
CONHMs	O	CH_2Ph	SO_2
NHMs	SO_2	CH_2CH_2Ph	SO_2
NO_2	SO_2	Me	SO
OH	SO_2	Et	SO
COMe	SO_2	iPr	SO
COOH	SO_2	nPr	SO



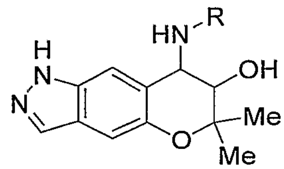
R^{13}	X	R^{13}	X
NO_2	O	Me	O
CHO	O	Et	O
SO_3H	O	iPr	O
Cl	O	nPr	O
Br	O	nBu	O
CH_2OH	O	tBu	O
CH_2NH_2	O	Ph	O
CH_2NHMe	O	CH_2Ph	O
CH_2Ph	SO	CH_2CH_2Ph	O
COMe	SO	Me	S
COOH	SO	Et	S
$CONH_2$	SO	iPr	S
CONHMe	SO	nPr	S
CONHMs	SO	nBu	S
NHMs	SO	tBu	S
NHCOMe	SO	Ph	S
NO_2	SO_2	CH_2Ph	S
CHO	S	CH_2CH_2Ph	S
SO_3H	S	Me	SO_2
SO_2NHMe	SO_2	Et	SO_2
OH	SO	iPr	SO_2
COMe	O	nPr	SO_2
COOH	O	nBu	SO_2
$CONH_2$	O	tBu	SO_2
CONHMe	O	Ph	SO_2
CONHMs	O	CH_2Ph	SO_2
NHMs	SO_2	CH_2CH_2Ph	SO_2
NO_2	SO_2	Me	SO
OH	SO_2	Et	SO
COMe	SO_2	iPr	SO
COOH	SO_2	nPr	SO



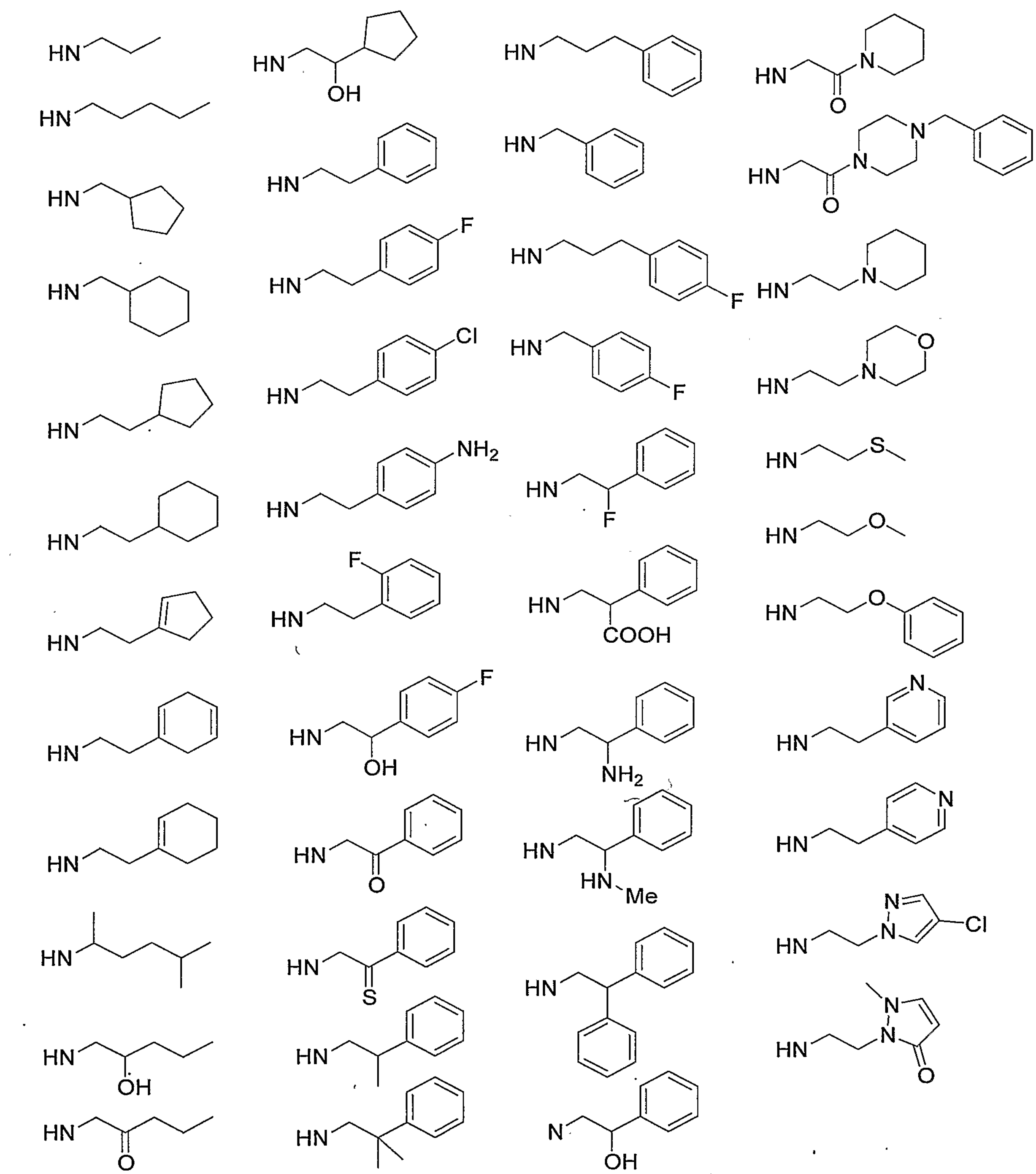
R^{13}	X	R^{13}	X
NO_2	O	Me	O
CHO	O	Et	O
SO_3H	O	iPr	O
Cl	O	nPr	O
Br	O	nBu	O
CH_2OH	O	tBu	O
CH_2NH_2	O	Ph	O
CH_2NHMe	O	CH_2Ph	O
CH_2Ph	SO	CH_2CH_2Ph	O
COMe	SO	Me	S
COOH	SO	Et	S
$CONH_2$	SO	iPr	S
CONHMe	SO	nPr	S
CONHMs	SO	nBu	S
NHMs	SO	tBu	S
NHCOMe	SO	Ph	S
NO_2	SO_2	CH_2Ph	S
CHO	S	CH_2CH_2Ph	S
SO_3H	S	Me	SO_2
SO_2NHMe	SO_2	Et	SO_2
OH	SO	iPr	SO_2
COMe	O	nPr	SO_2
COOH	O	nBu	SO_2
$CONH_2$	O	tBu	SO_2
CONHMe	O	Ph	SO_2
CONHMs	O	CH_2Ph	SO_2
NHMs	SO_2	CH_2CH_2Ph	SO_2
NO_2	SO_2	Me	SO
OH	SO_2	Et	SO
COMe	SO_2	iPr	SO
COOH	SO_2	nPr	SO

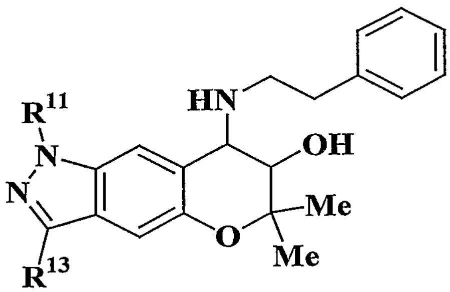


R^{13}	X	R^{13}	X
NO_2	O	Me	O
CHO	O	Et	O
SO_3H	O	iPr	O
Cl	O	nPr	O
Br	O	nBu	O
CH_2OH	O	tBu	O
CH_2NH_2	O	Ph	O
CH_2NHMe	O	CH_2Ph	O
CH_2Ph	SO	CH_2CH_2Ph	O
COMe	SO	Me	S
COOH	SO	Et	S
$CONH_2$	SO	iPr	S
CONHMe	SO	nPr	S
CONHMs	SO	nBu	S
NHMs	SO	tBu	S
NHCOMe	SO	Ph	S
NO_2	SO_2	CH_2Ph	S
CHO	S	CH_2CH_2Ph	S
SO_3H	S	Me	SO_2
SO_2NHMe	SO_2	Et	SO_2
OH	SO	iPr	SO_2
COMe	O	nPr	SO_2
COOH	O	nBu	SO_2
$CONH_2$	O	tBu	SO_2
CONHMe	O	Ph	SO_2
CONHMs	O	CH_2Ph	SO_2
NHMs	SO_2	CH_2CH_2Ph	SO_2
NO_2	SO_2	Me	SO
OH	SO_2	Et	SO
COMe	SO_2	iPr	SO
COOH	SO_2	nPr	SO

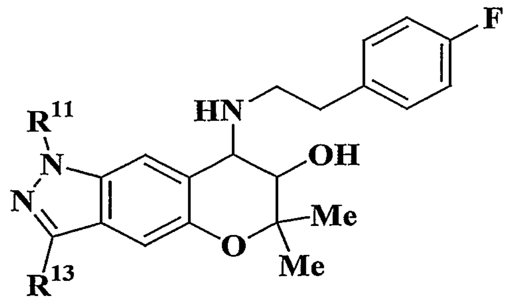


HN—R

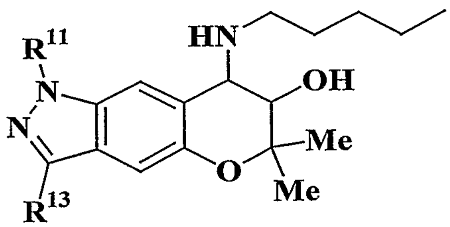




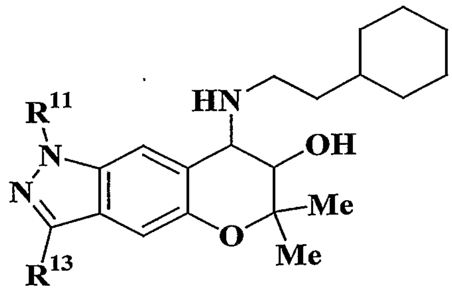
R^{11}	R^{13}
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
Me	Ph
Me	NO_2
Me	CHO
Me	SO_3H
Me	Cl
Me	Br
Et	CH_2OH
Et	CH_2NH_2
Et	CH_2NHMe
iPr	CH_2Ph
nPr	COMe
nBu	COOH
tBu	$CONH_2$
Ph	CONHMe
CH_2OH	CONHMs
CH_2OH	NHMs
CH_2OMe	NHCOMe
CH_2OMe	NO_2
CH_2NH_2	CHO
CH_2NH_2	nPr
CH_2NH_2	Cl
CH_2NH_2	F
CH_2NHMe	Cl
CH_2Ph	Et
CH_2Ph	nPr
CH_2CH_2Ph	Ph



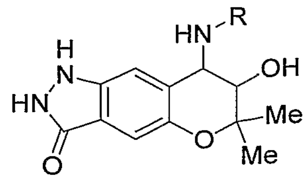
R^{11}	R^{13}
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
Me	Ph
Me	NO_2
Me	CHO
Me	SO_3H
Me	Cl
Me	Br
Et	CH_2OH
Et	CH_2NH_2
Et	CH_2NHMe
iPr	CH_2Ph
nPr	COMe
nBu	COOH
tBu	$CONH_2$
Ph	CONHMe
CH_2OH	CONHMs
CH_2OH	NHMs
CH_2OMe	NHCOMe
CH_2OMe	NO_2
CH_2NH_2	CHO
CH_2NH_2	nPr
CH_2NH_2	Cl
CH_2NH_2	F
CH_2NHMe	Cl
CH_2Ph	Et
CH_2Ph	nPr
CH_2CH_2Ph	Ph



R^{11}	R^{13}
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
Me	Ph
Me	NO_2
Me	CHO
Me	SO_3H
Me	Cl
Me	Br
Et	CH_2OH
Et	CH_2NH_2
Et	CH_2NHMe
iPr	CH_2Ph
nPr	COMe
nBu	COOH
tBu	$CONH_2$
Ph	CONHMe
CH_2OH	CONHMs
CH_2OH	NHMs
CH_2OMe	NHCOMe
CH_2OMe	NO_2
CH_2NH_2	CHO
CH_2NH_2	nPr
CH_2NH_2	Cl
CH_2NH_2	F
CH_2NHMe	Cl
CH_2Ph	Et
CH_2Ph	nPr
CH_2CH_2Ph	Ph



R^{11}	R^{13}
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
Me	Ph
Me	NO_2
Me	CHO
Me	SO_3H
Me	Cl
Me	Br
Et	CH_2OH
Et	CH_2NH_2
Et	CH_2NHMe
iPr	CH_2Ph
nPr	COMe
nBu	COOH
tBu	$CONH_2$
Ph	CONHMe
CH_2OH	CONHMs
CH_2OH	NHMs
CH_2OMe	NHCOMe
CH_2OMe	NO_2
CH_2NH_2	CHO
CH_2NH_2	nPr
CH_2NH_2	Cl
CH_2NH_2	F
CH_2NHMe	Cl
CH_2Ph	Et
CH_2Ph	nPr
CH_2CH_2Ph	Ph



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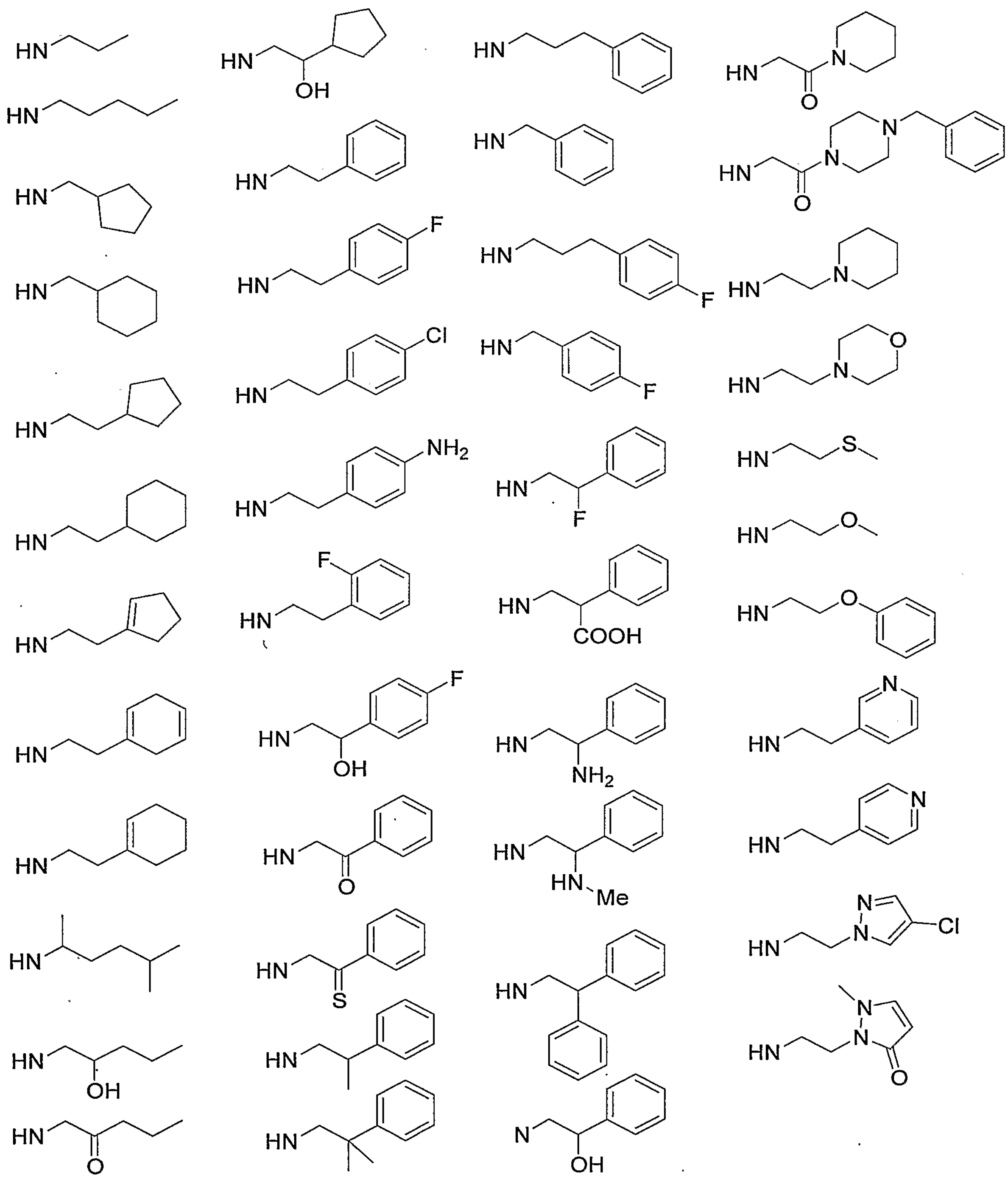

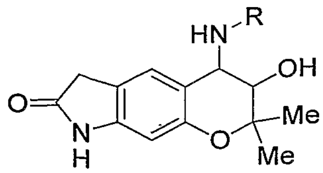

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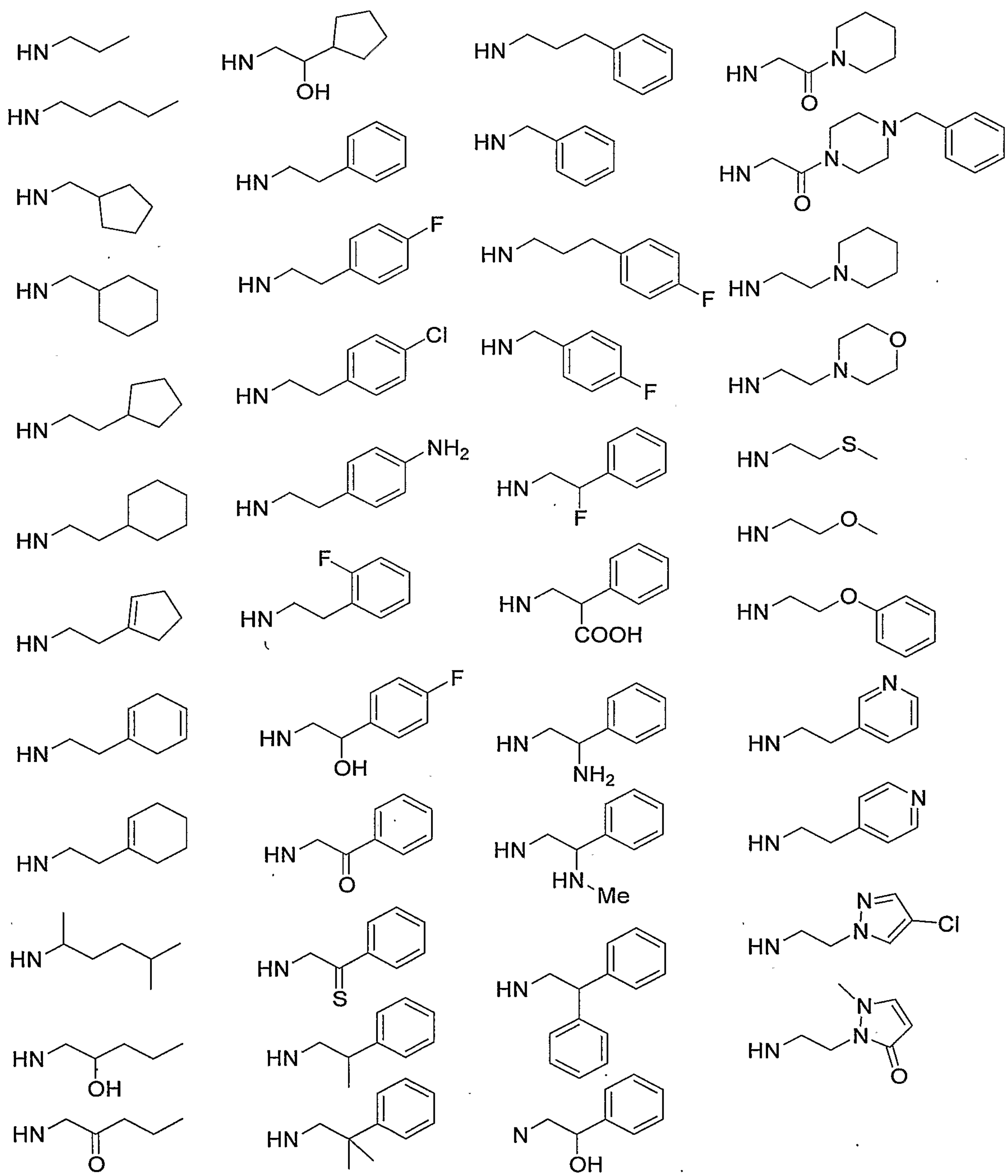

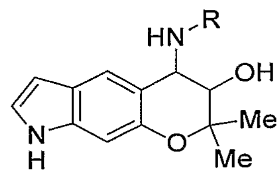

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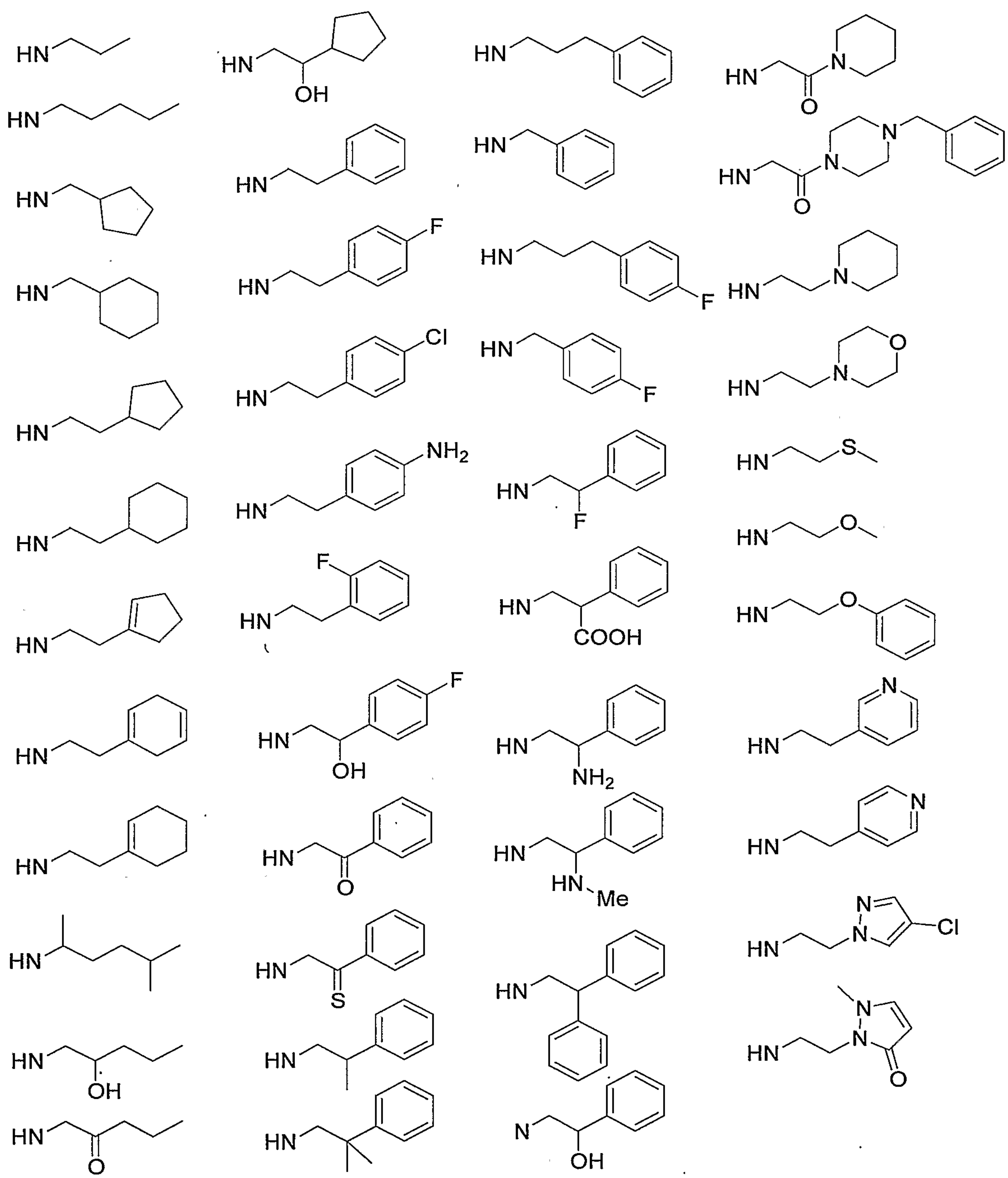

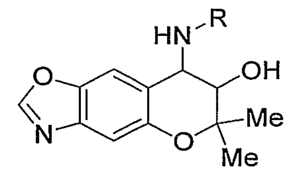

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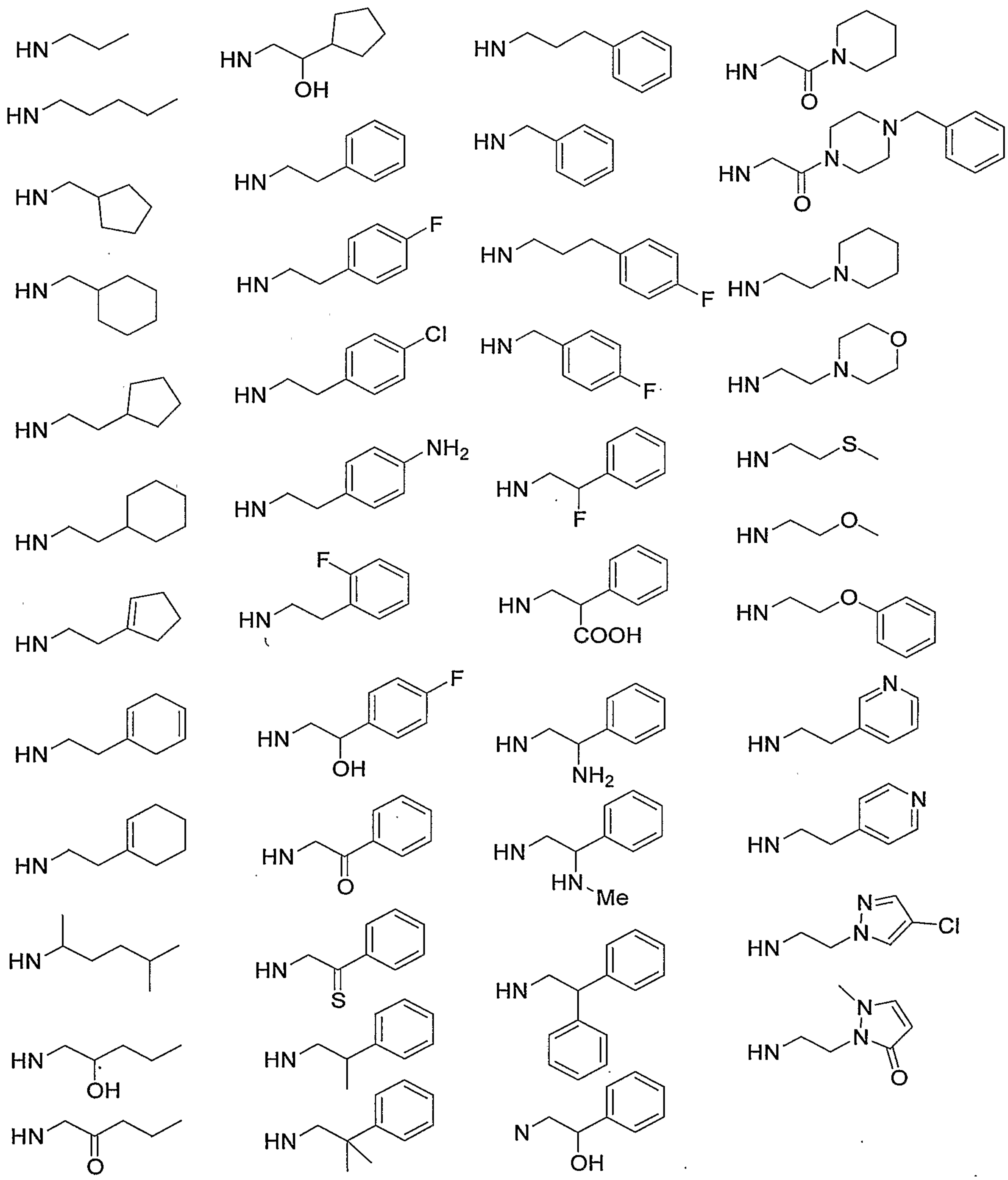

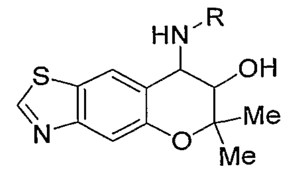

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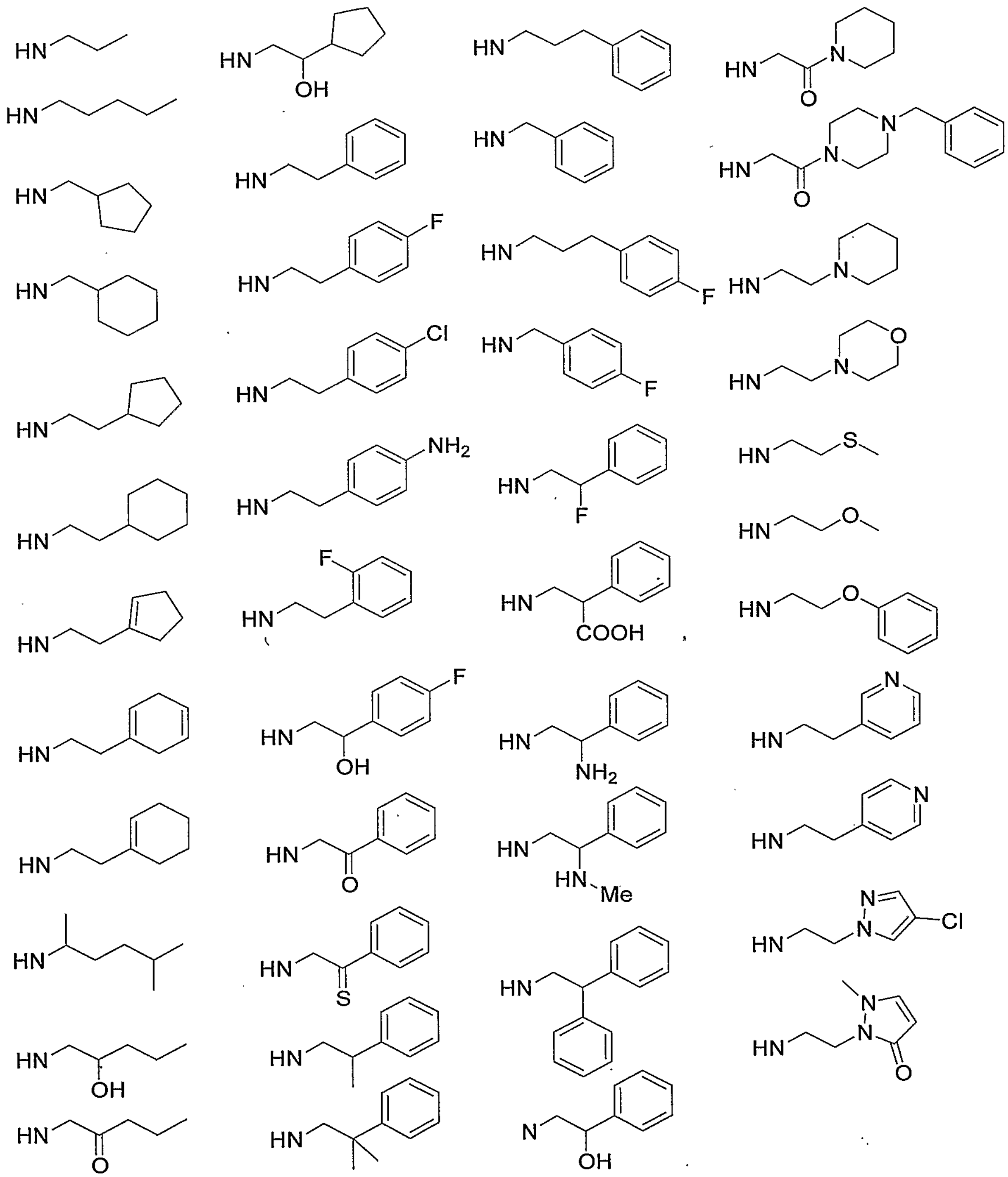

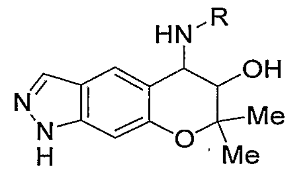

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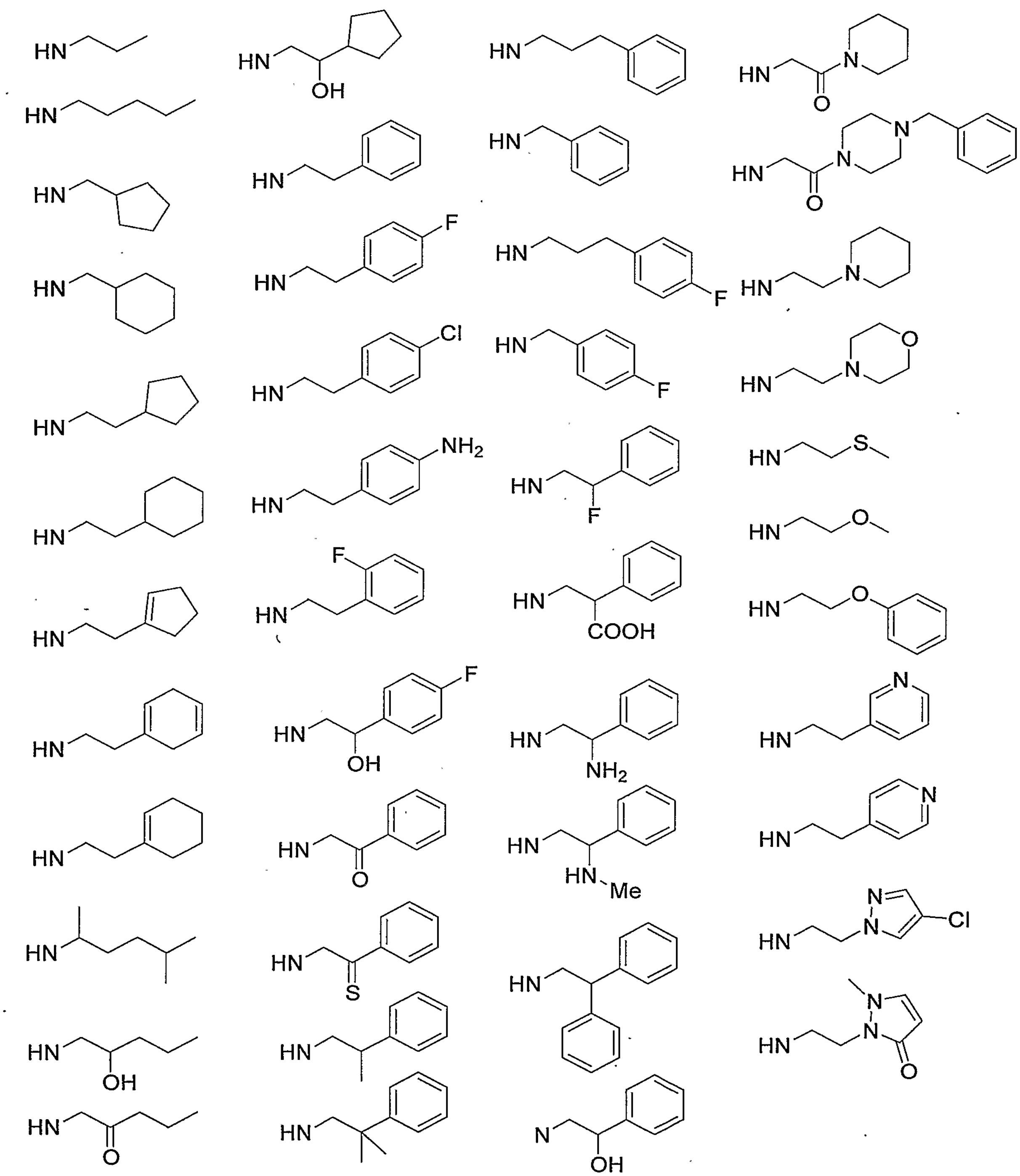

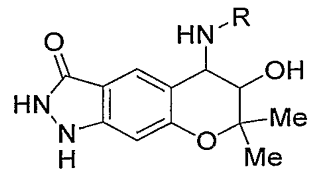

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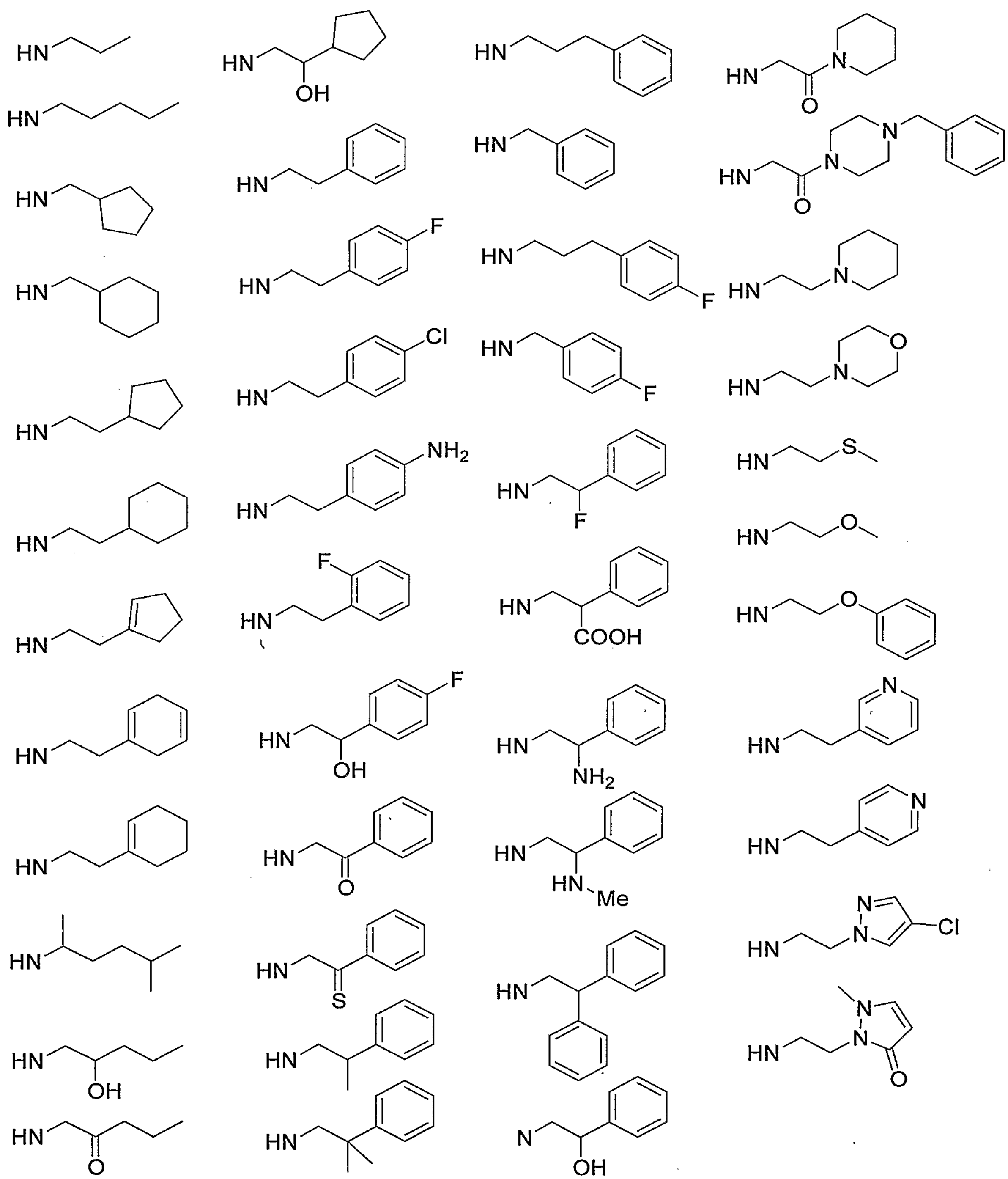

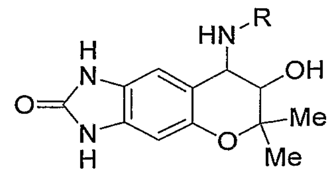

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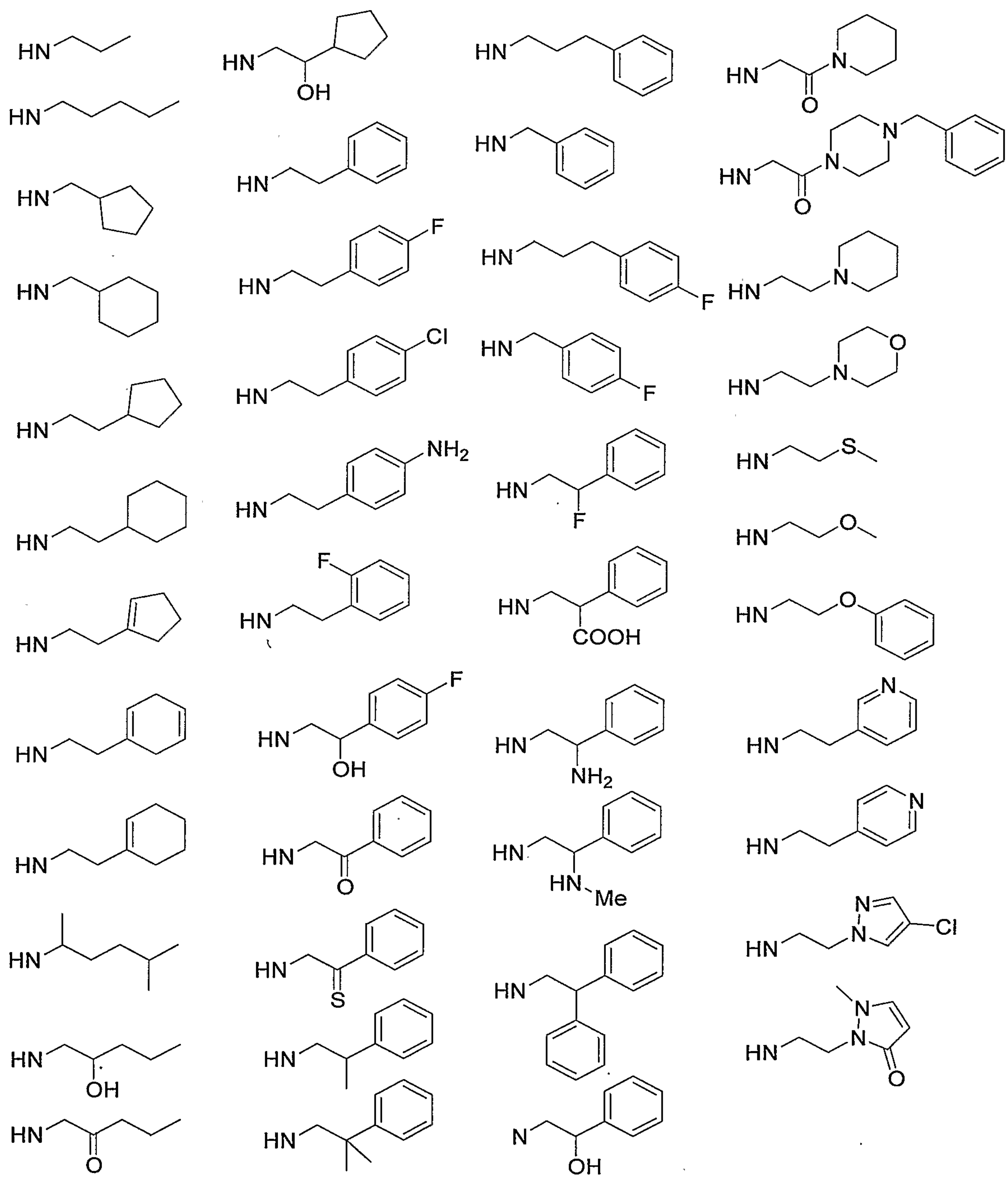
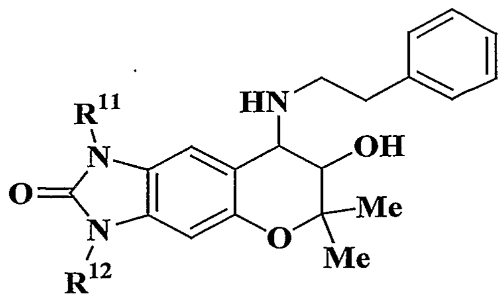
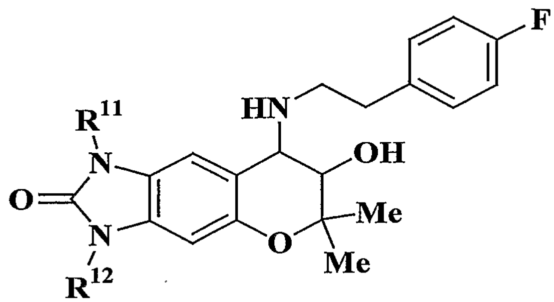
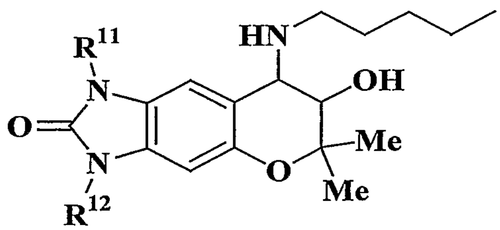




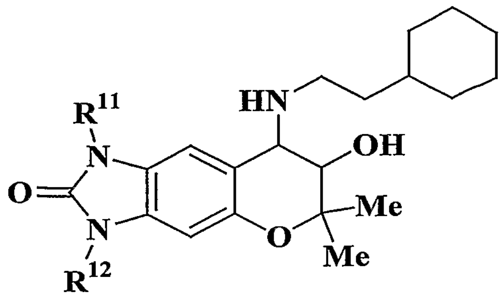
R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



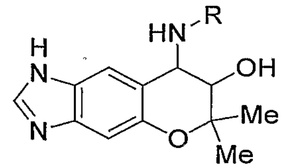
R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



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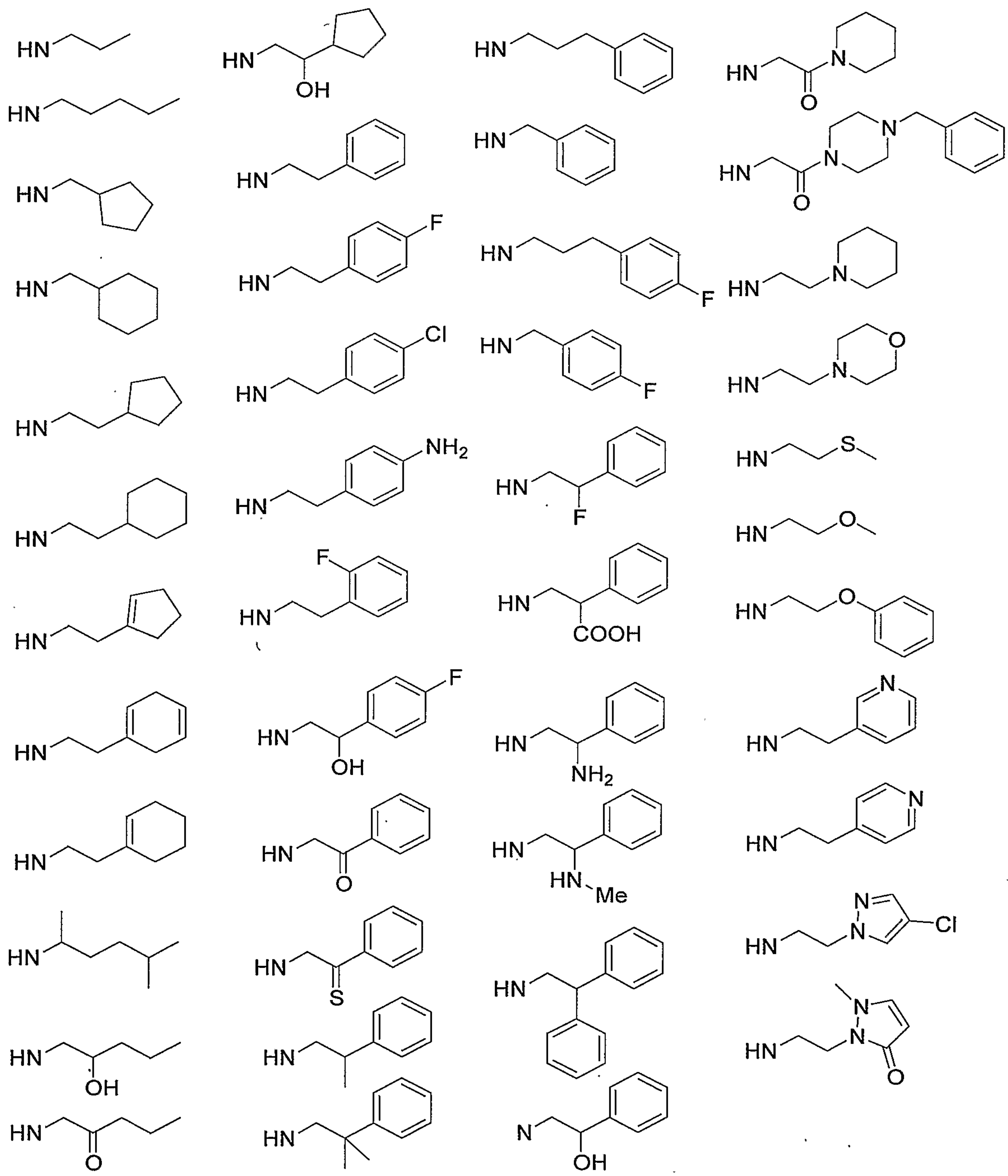
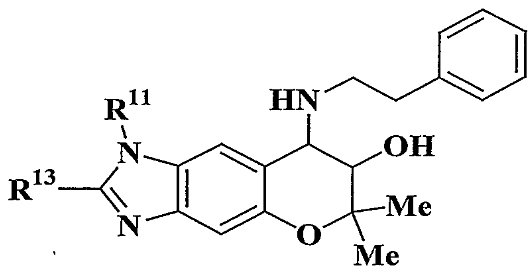
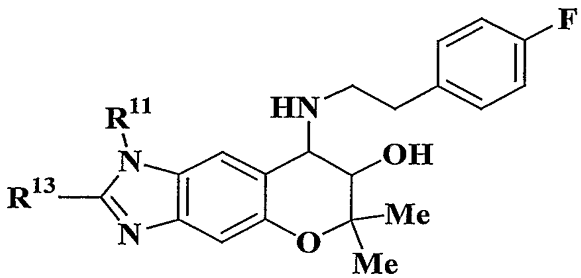
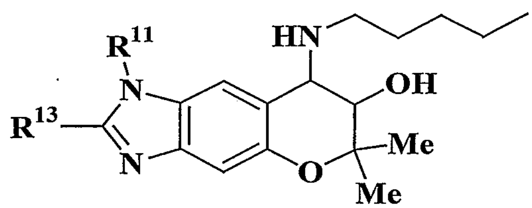




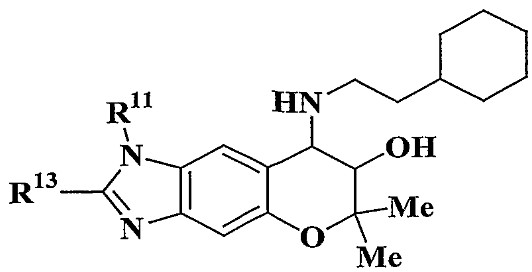
R^{11}	R^{13}	R^{11}	R^{13}
H	Me	H	NO_2
H	Et	H	CHO
H	iPr	H	SO_3H
H	nPr	H	Cl
H	nBu	H	Br
H	tBu	Me	CH_2OH
H	Ph	Me	CH_2NH_2
Me	Me	Me	CH_2NHMe
Me	Et	Me	CH_2Ph
Et	iPr	Me	COMe
Et	nPr	Me	COOH
iPr	nBu	Et	$CONH_2$
nPr	tBu	Et	CONHMe
nBu	Ph	Et	CONHMs
tBu	iPr	iPr	NHMs
Ph	nPr	nPr	NHCOMe
CH_2OH	nBu	nBu	NO_2
CH_2OH	tBu	tBu	CHO
CH_2OMe	Ph	Ph	SO_3H
CH_2OMe	Et	CH_2OH	SO_2NHMe
CH_2NH_2	nPr	CH_2OH	OH
CH_2NH_2	Ph	CH_2OMe	COMe
CH_2NH_2	Cl	CH_2OMe	COOH
CH_2NH_2	F	CH_2NH_2	$CONH_2$
CH_2NHMe	Cl	CH_2NH_2	CONHMe
CH_2Ph	Et	CH_2NH_2	CONHMs
CH_2Ph	nPr	CH_2NH_2	NHMs
CH_2Ph	Ph	CH_2NHMe	NO_2
CH_2CH_2Ph	Me	CH_2Ph	OH
H	CH_2Ph	CH_2Ph	COMe
Me	CH_2Ph	CH_2CH_2Ph	COOH



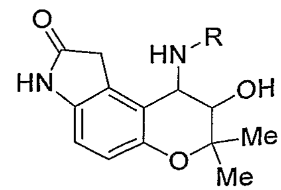
R^{11}	R^{13}	R^{11}	R^{13}
H	Me	H	NO_2
H	Et	H	CHO
H	iPr	H	SO_3H
H	nPr	H	Cl
H	nBu	H	Br
H	tBu	Me	CH_2OH
H	Ph	Me	CH_2NH_2
Me	Me	Me	CH_2NHMe
Me	Et	Me	CH_2Ph
Et	iPr	Me	COMe
Et	nPr	Me	COOH
iPr	nBu	Et	$CONH_2$
nPr	tBu	Et	CONHMe
nBu	Ph	Et	CONHMs
tBu	iPr	iPr	NHMs
Ph	nPr	nPr	NHCOMe
CH_2OH	nBu	nBu	NO_2
CH_2OH	tBu	tBu	CHO
CH_2OMe	Ph	Ph	SO_3H
CH_2OMe	Et	CH_2OH	SO_2NHMe
CH_2NH_2	nPr	CH_2OH	OH
CH_2NH_2	Ph	CH_2OMe	COMe
CH_2NH_2	Cl	CH_2OMe	COOH
CH_2NH_2	F	CH_2NH_2	$CONH_2$
CH_2NHMe	Cl	CH_2NH_2	CONHMe
CH_2Ph	Et	CH_2NH_2	CONHMs
CH_2Ph	nPr	CH_2NH_2	NHMs
CH_2Ph	Ph	CH_2NHMe	NO_2
CH_2CH_2Ph	Me	CH_2Ph	OH
H	CH_2Ph	CH_2Ph	COMe
Me	CH_2Ph	CH_2CH_2Ph	COOH



R^{11}	R^{13}	R^{11}	R^{13}
H	Me	H	NO_2
H	Et	H	CHO
H	iPr	H	SO_3H
H	nPr	H	Cl
H	nBu	H	Br
H	tBu	Me	CH_2OH
H	Ph	Me	CH_2NH_2
Me	Me	Me	CH_2NHMe
Me	Et	Me	CH_2Ph
Et	iPr	Me	COMe
Et	nPr	Me	COOH
iPr	nBu	Et	$CONH_2$
nPr	tBu	Et	CONHMe
nBu	Ph	Et	CONHMs
tBu	iPr	iPr	NHMs
Ph	nPr	nPr	NHCOMe
CH_2OH	nBu	nBu	NO_2
CH_2OH	tBu	tBu	CHO
CH_2OMe	Ph	Ph	SO_3H
CH_2OMe	Et	CH_2OH	SO_2NHMe
CH_2NH_2	nPr	CH_2OH	OH
CH_2NH_2	Ph	CH_2OMe	COMe
CH_2NH_2	Cl	CH_2OMe	COOH
CH_2NH_2	F	CH_2NH_2	$CONH_2$
CH_2NHMe	Cl	CH_2NH_2	CONHMe
CH_2Ph	Et	CH_2NH_2	CONHMs
CH_2Ph	nPr	CH_2NH_2	NHMs
CH_2Ph	Ph	CH_2NHMe	NO_2
CH_2CH_2Ph	Me	CH_2Ph	OH
H	CH_2Ph	CH_2Ph	COMe
Me	CH_2Ph	CH_2CH_2Ph	COOH



R^{11}	R^{13}	R^{11}	R^{13}
H	Me	H	NO_2
H	Et	H	CHO
H	iPr	H	SO_3H
H	nPr	H	Cl
H	nBu	H	Br
H	tBu	Me	CH_2OH
H	Ph	Me	CH_2NH_2
Me	Me	Me	CH_2NHMe
Me	Et	Me	CH_2Ph
Et	iPr	Me	COMe
Et	nPr	Me	COOH
iPr	nBu	Et	$CONH_2$
nPr	tBu	Et	CONHMe
nBu	Ph	Et	CONHMs
tBu	iPr	iPr	NHMs
Ph	nPr	nPr	NHCOMe
CH_2OH	nBu	nBu	NO_2
CH_2OH	tBu	tBu	CHO
CH_2OMe	Ph	Ph	SO_3H
CH_2OMe	Et	CH_2OH	SO_2NHMe
CH_2NH_2	nPr	CH_2OH	OH
CH_2NH_2	Ph	CH_2OMe	COMe
CH_2NH_2	Cl	CH_2OMe	COOH
CH_2NH_2	F	CH_2NH_2	$CONH_2$
CH_2NHMe	Cl	CH_2NH_2	CONHMe
CH_2Ph	Et	CH_2NH_2	CONHMs
CH_2Ph	nPr	CH_2NH_2	NHMs
CH_2Ph	Ph	CH_2NHMe	NO_2
CH_2CH_2Ph	Me	CH_2Ph	OH
H	CH_2Ph	CH_2Ph	COMe
Me	CH_2Ph	CH_2CH_2Ph	COOH



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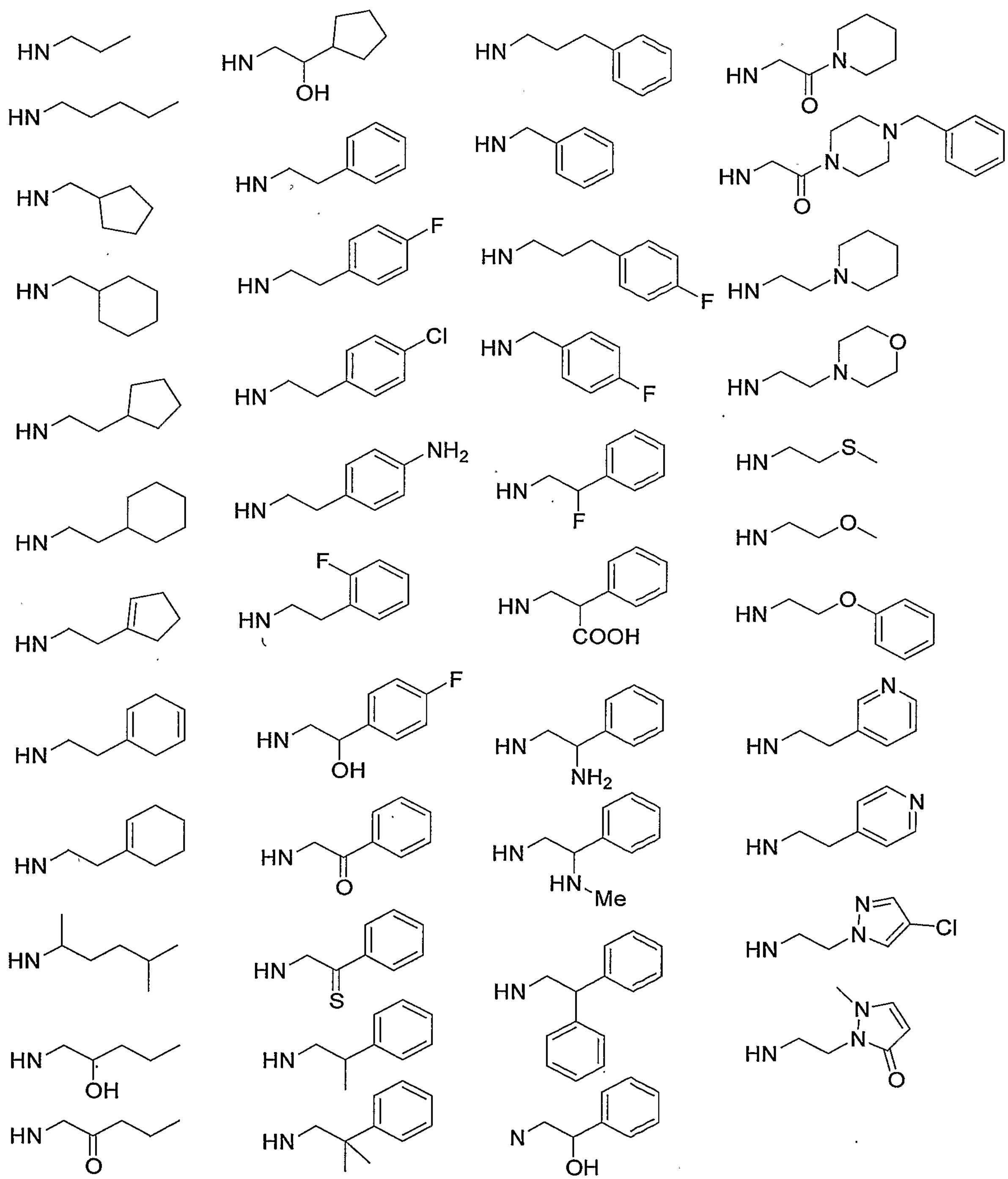

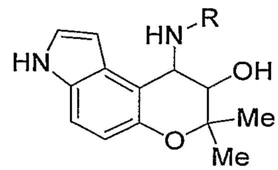

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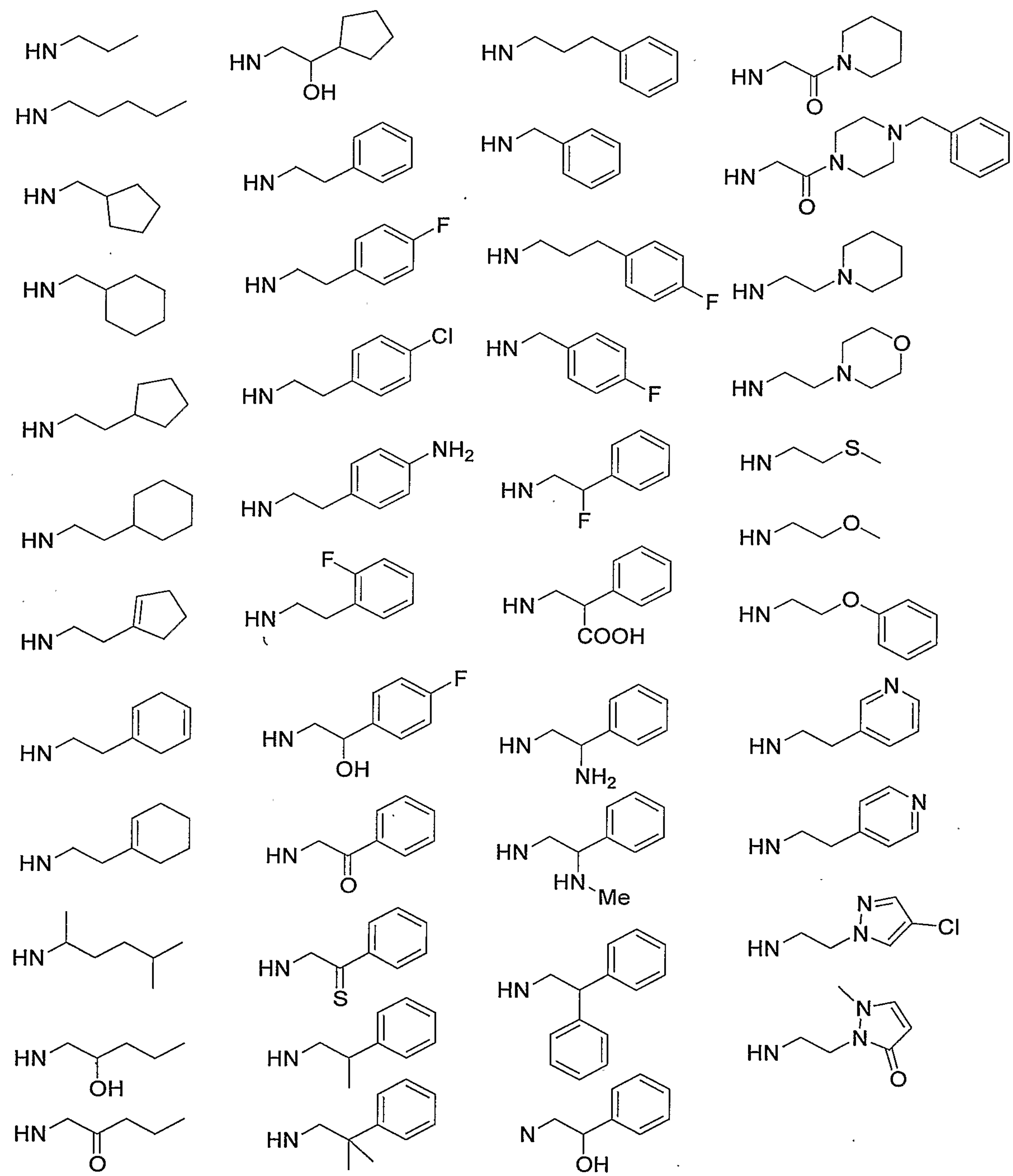

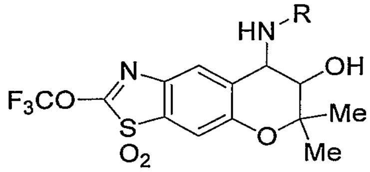

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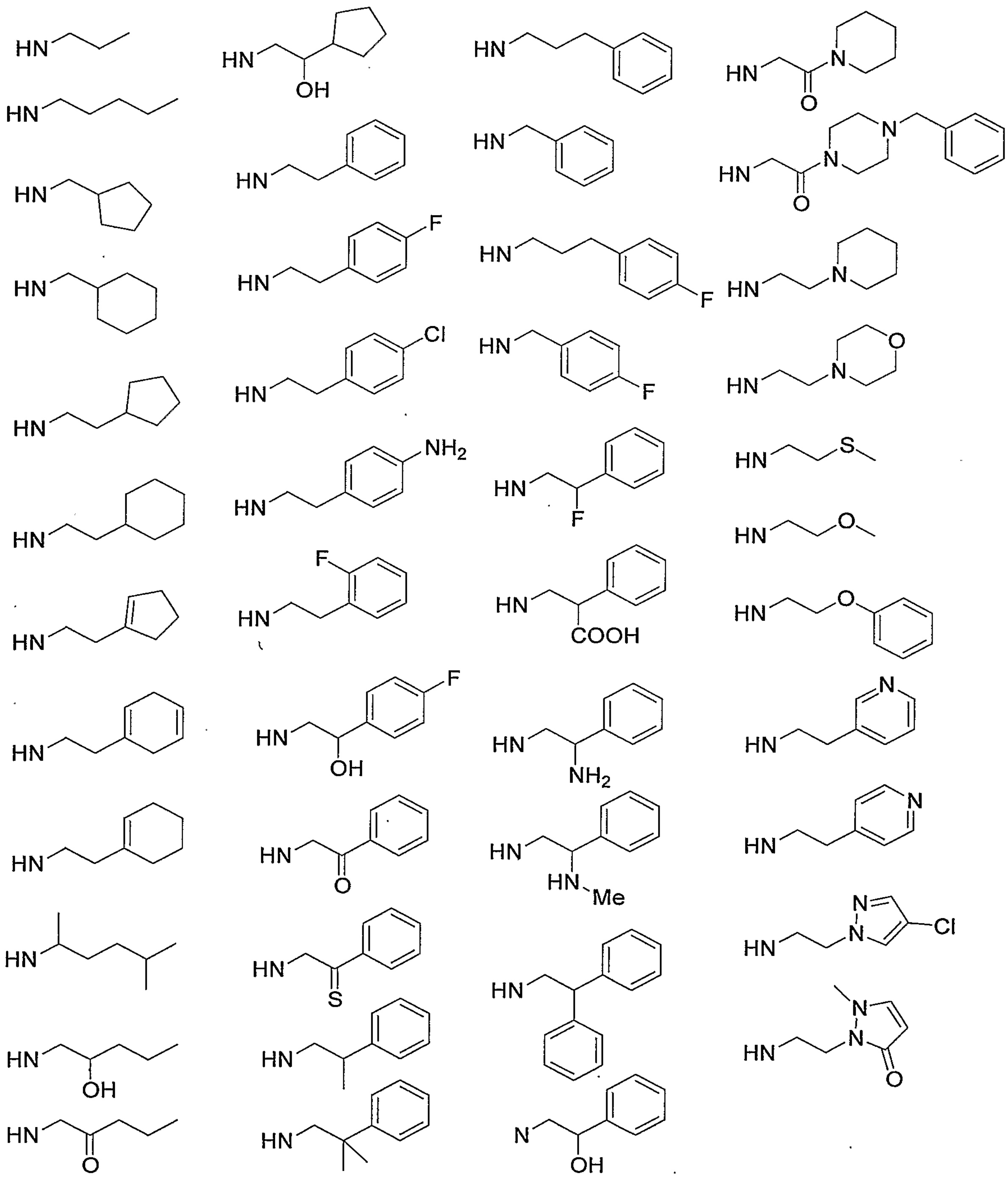

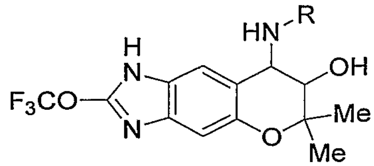

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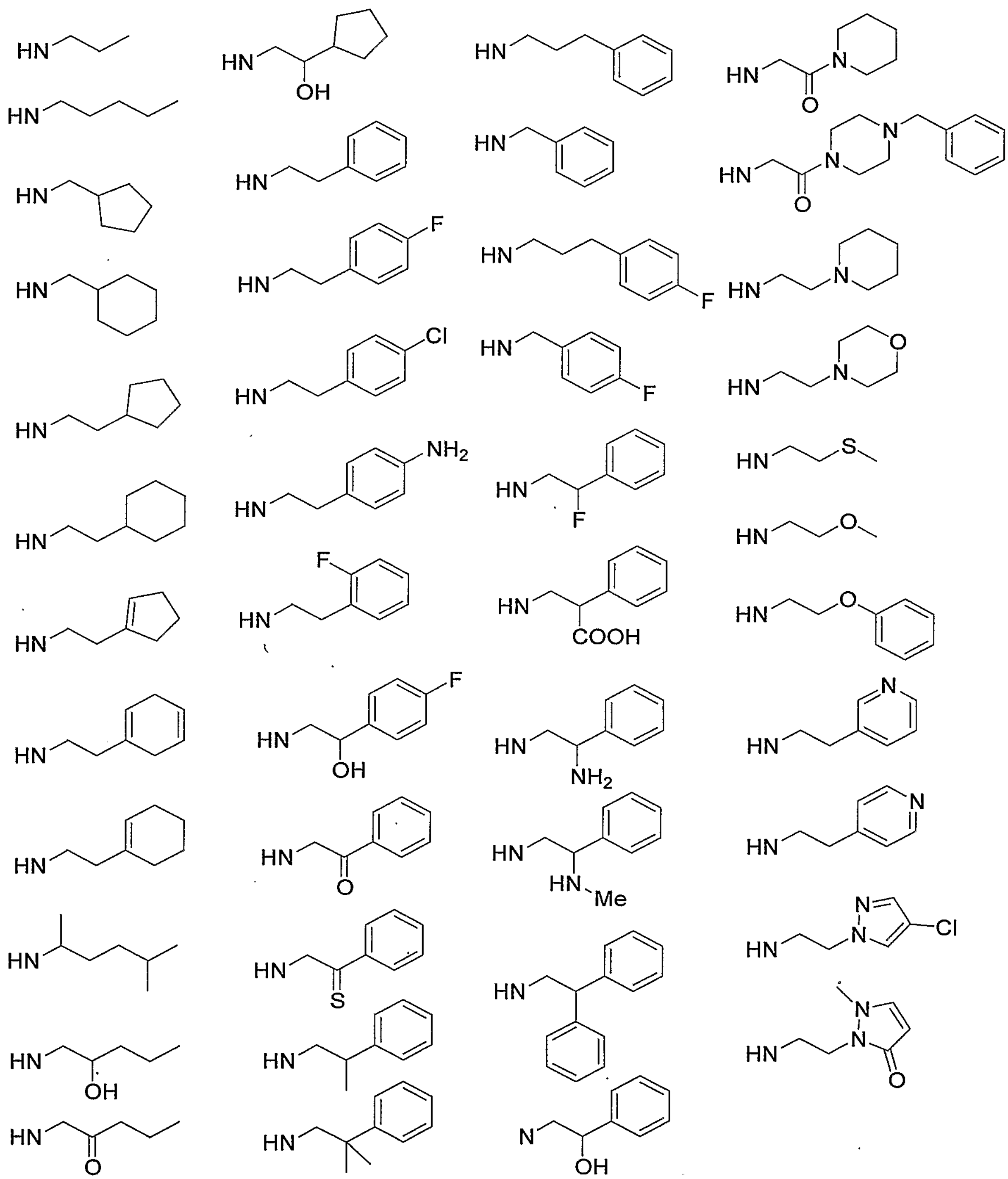
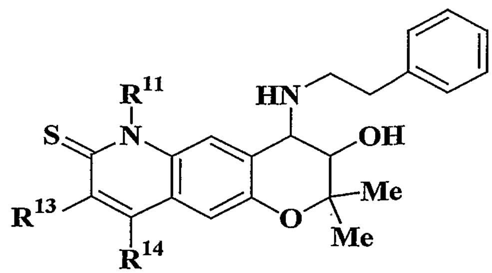
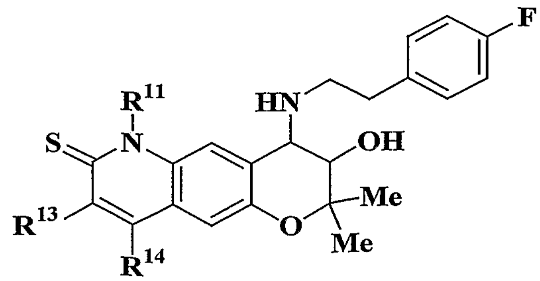




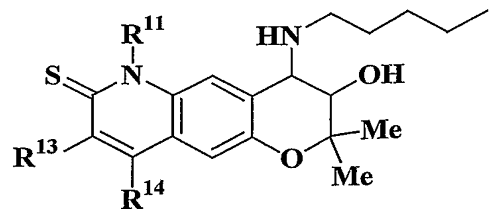
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	H
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

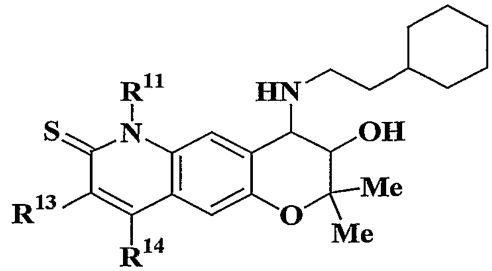
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2H
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2H
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



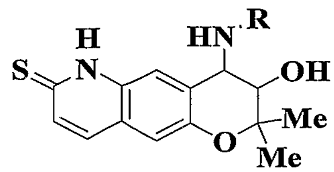
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	H
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



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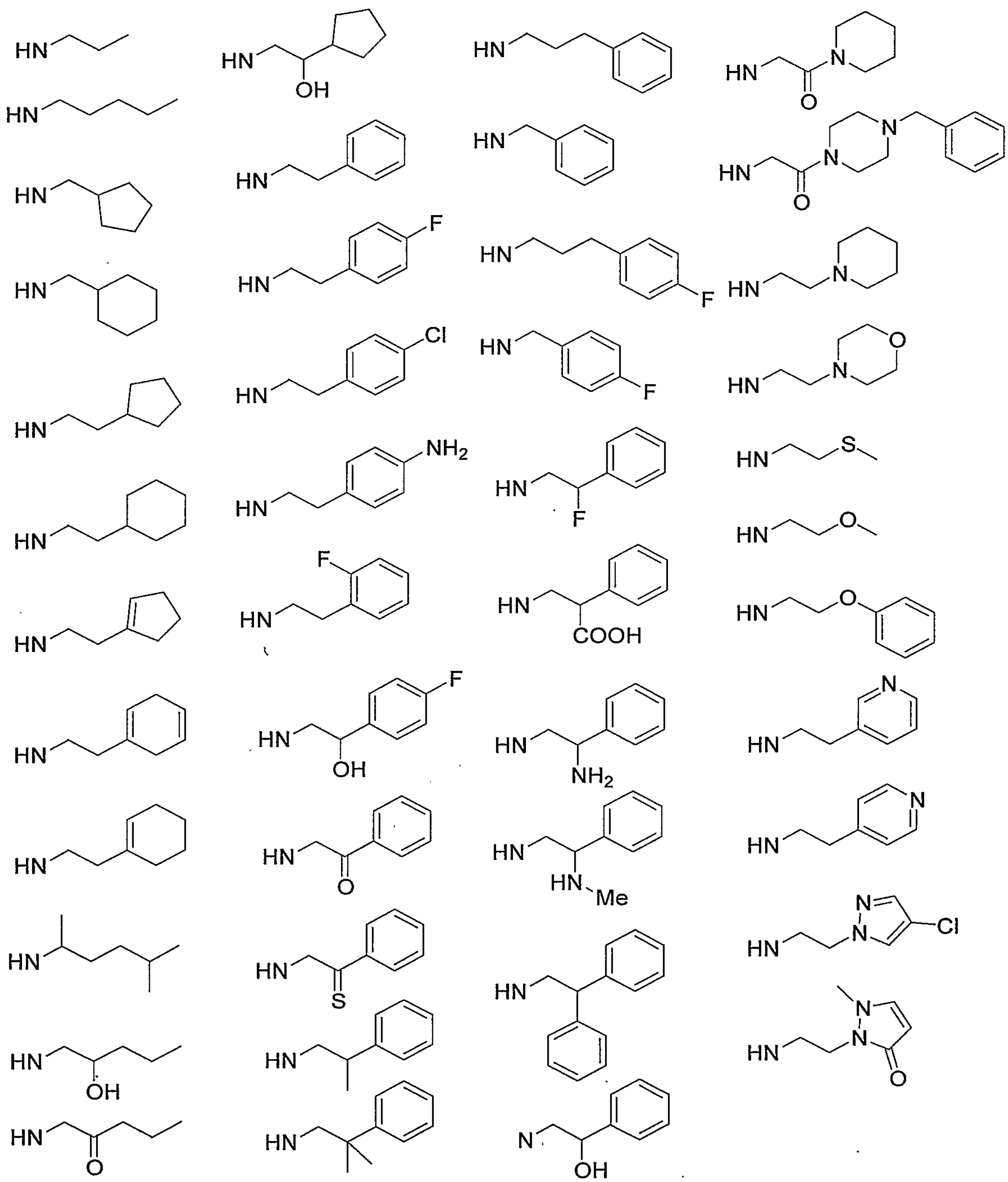
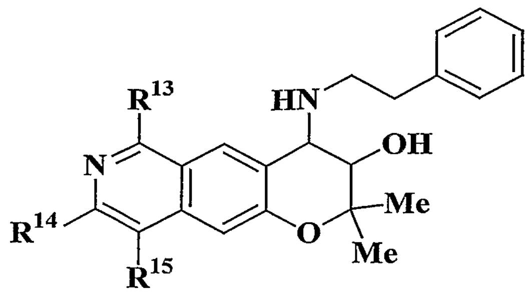
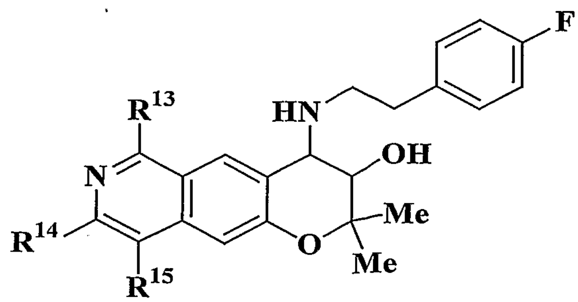
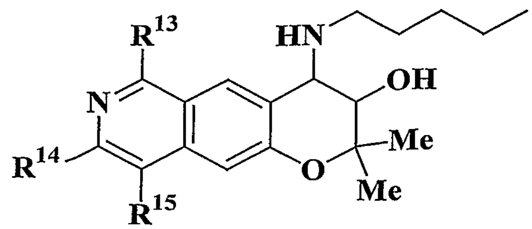




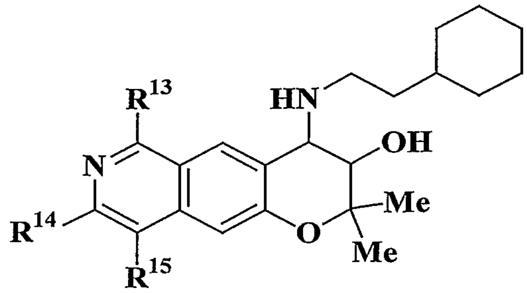
R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



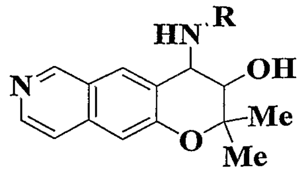
R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2H	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2H	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



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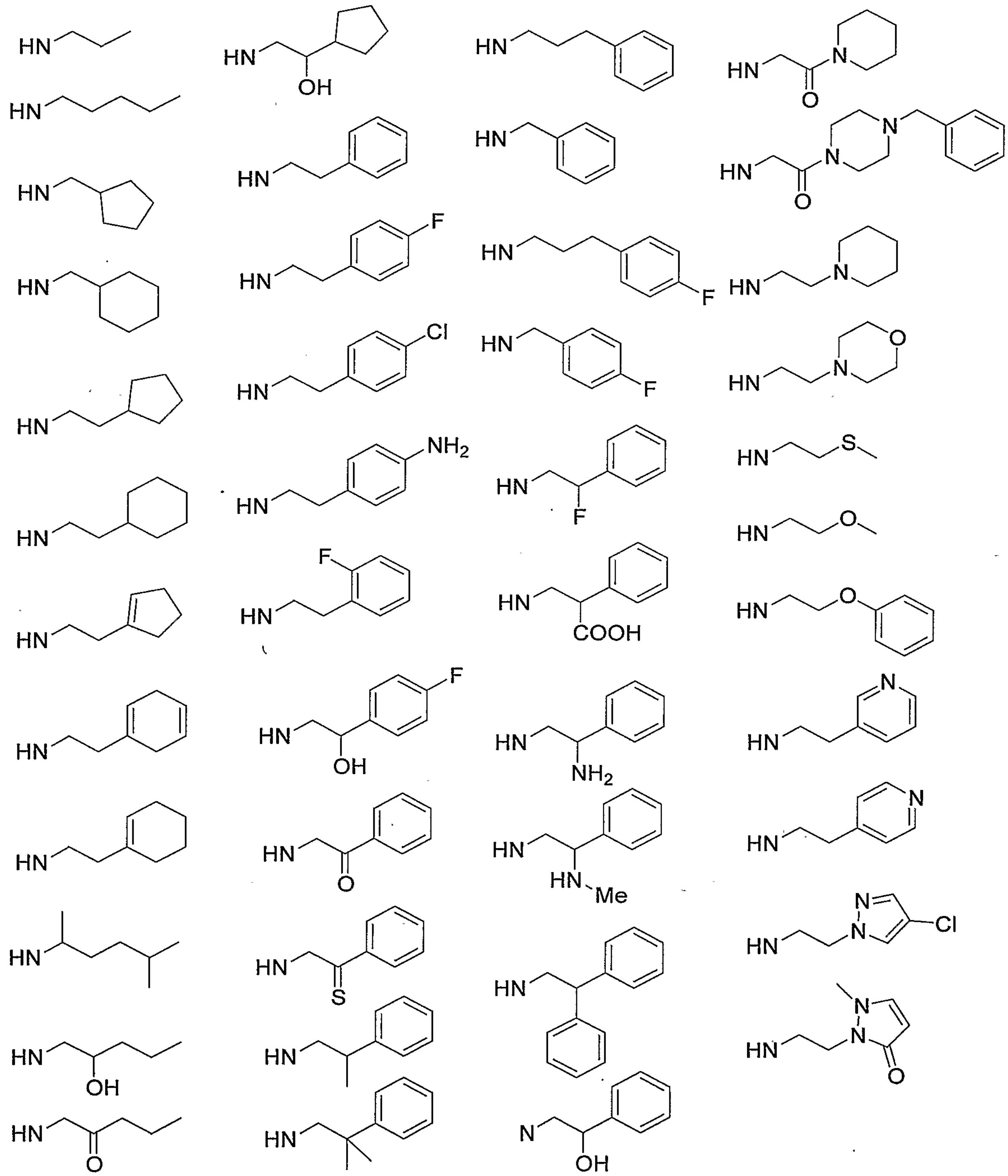
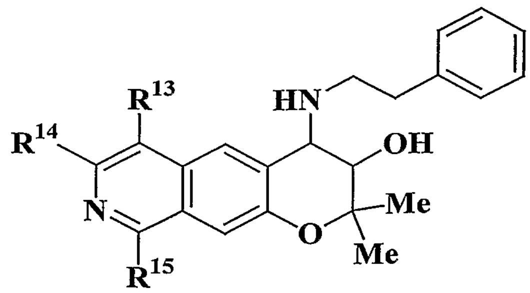
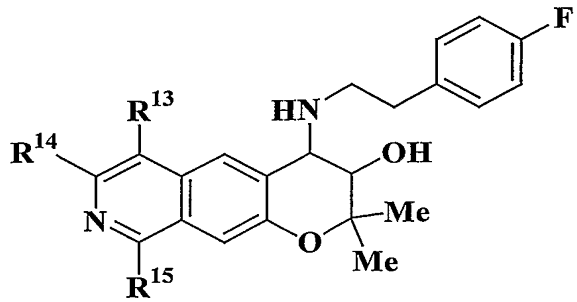
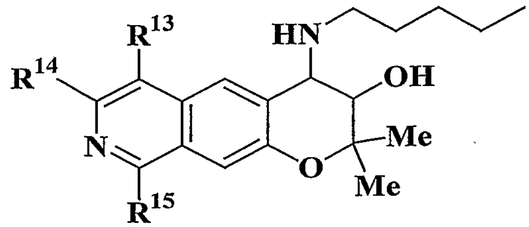




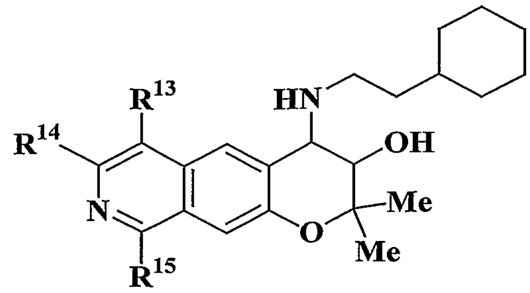
R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



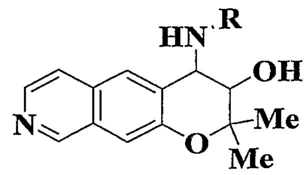
R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



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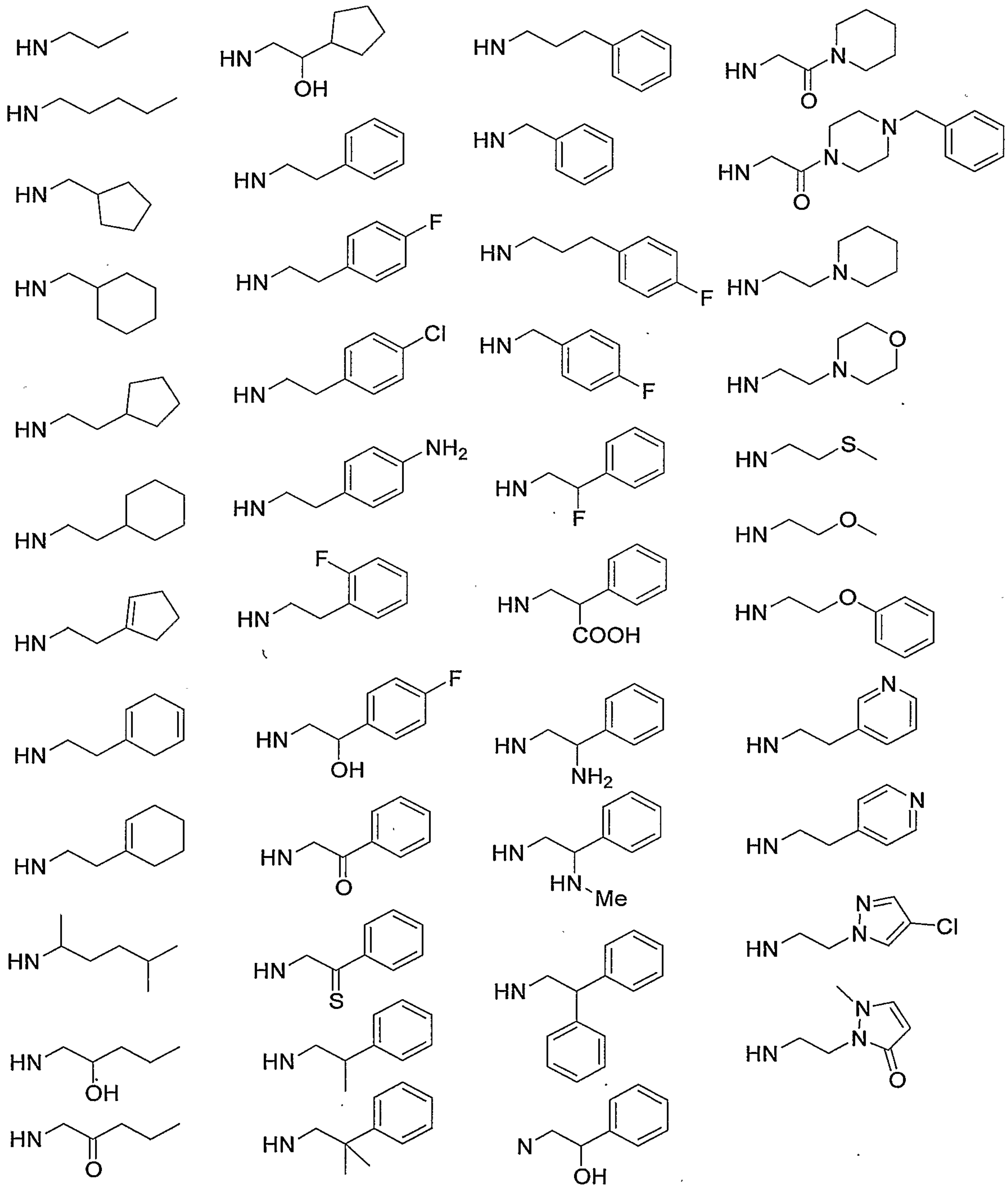
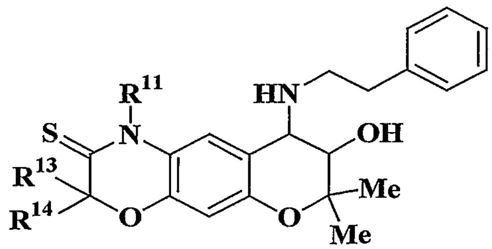
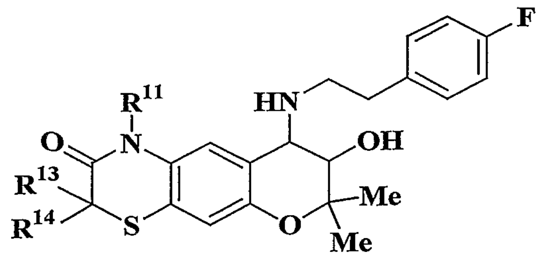
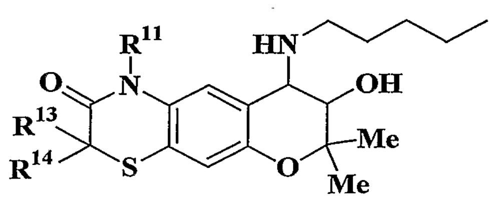




R11	R13	R14	R11	R13	R14	R11	R13	R14
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



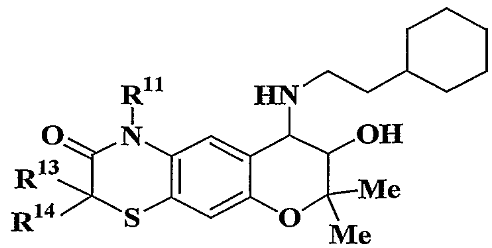
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



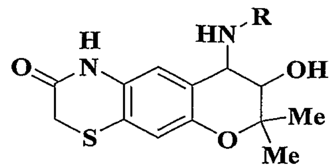
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



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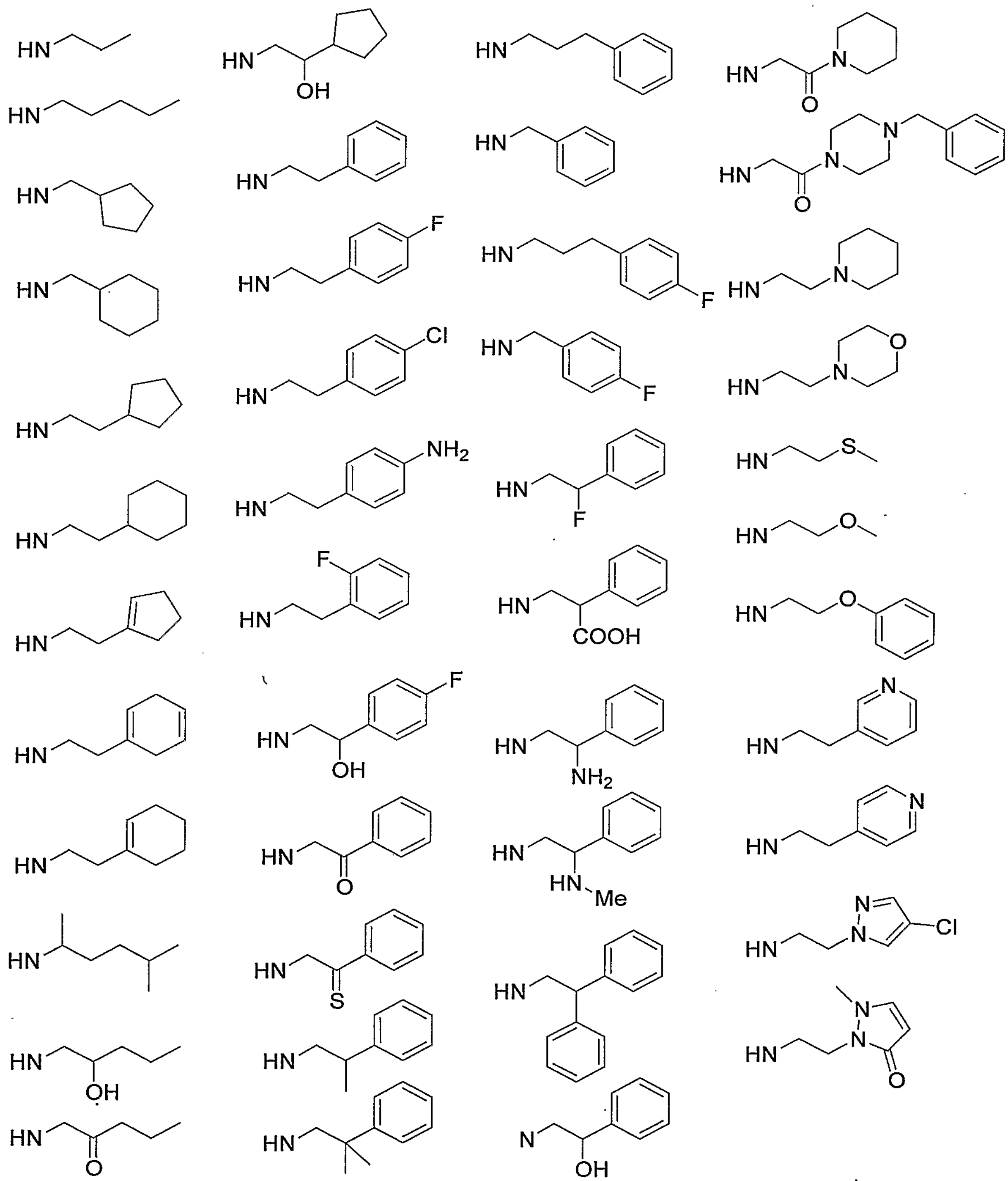
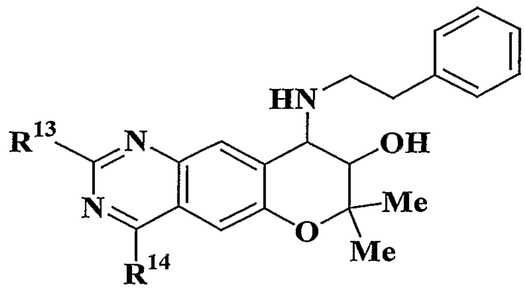
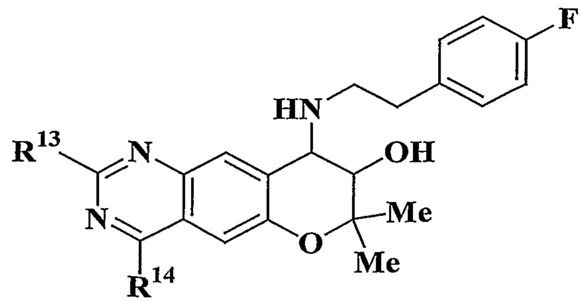




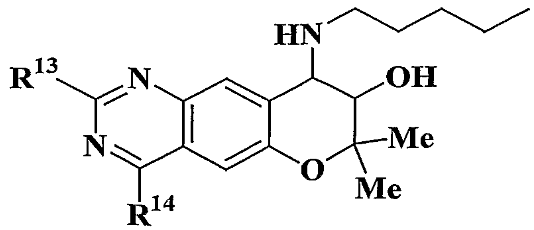
R^{13}	R^{14}	R^{13}	R^{14}	R^{13}	R^{14}
H	Me	NO_2	H	OMe	H
H	Et	CHO	H	OEt	H
H	iPr	SO_3H	H	OiPr	H
H	nPr	Cl	H	OnPr	H
H	nBu	Br	H	OBn	H
H	tBu	CH_2OH	H	OPh	H
H	Ph	CH_2NH_2	H	SMe	H
Me	H	CH_2NHMe	H	SEt	H
Et	H	CH_2Ph	H	SiPr	H
iPr	H	COMe	H	SnPr	H
nPr	H	COOH	H	OCH_2CH_2Ph	H
nBu	H	$CONH_2$	H	SCH_2CH_2Ph	H
tBu	H	CONHMe	Et	H	OMe
Ph	NO_2	CONHMs	iPr	H	OEt
H	CHO	NHMs	nPr	Cl	OiPr
H	SO_3H	NHCOMe	nBu	Me	OnPr
H	Cl	NO_2	tBu	Et	OBn
H	Br	CHO	Ph	nPr	OPh
H	CH_2OH	SO_3H	Et	Ph	SMe
H	CH_2NH_2	SO_2NHMe	nPr	Me	SEt
Cl	CH_2NHMe	OH	Ph	Et	SiPr
Cl	CH_2Ph	COMe	Cl	nPr	SnPr
Cl	COMe	COOH	Cl	Ph	OCH_2CH_2Ph
Et	COOH	$CONH_2$	Cl	NO_2	SCOMe
nPr	$CONH_2$	CONHMe	Et	CHO	OMe
Ph	CONHMe	CONHMs	nPr	SO_3H	OEt
H	CONHMs	NHMs	Ph	Cl	OnPr
H	NHMs	NO_2	Me	Br	SMe
H	NHCOMe	OH	Et	CH_2OH	SEt
Me	CO_2H	COMe	nPr	CH_2NH_2	SiPr
Et	H	COOH	Ph	F	SPh



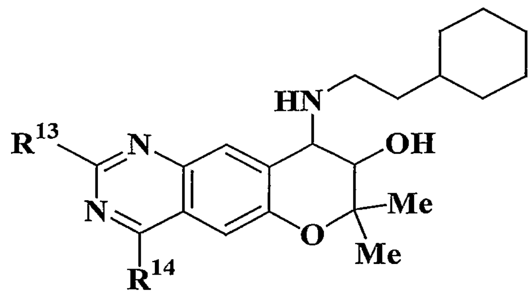
R^{13}	R^{14}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
H	Ph
Me	H
Et	H
iPr	H
nPr	H
nBu	H
tBu	H
Ph	NO_2
H	CHO
H	SO_3H
H	Cl
H	Br
H	CH_2OH
H	CH_2NH_2
Cl	CH_2NHMe
Cl	CH_2Ph
Cl	COMe
Et	COOH
nPr	$CONH_2$
Ph	CONHMe
H	CONHMs
H	NHMs
H	NHCOMe
Me	CO_2H
Et	H

R^{13}	R^{14}
NO_2	H
CHO	H
SO_3H	H
Cl	H
Br	H
CH_2OH	H
CH_2NH_2	H
CH_2NHMe	H
CH_2Ph	H
COMe	H
COOH	H
$CONH_2$	H
CONHMe	Et
CONHMs	iPr
NHMs	nPr
NHCOMe	nBu
NO_2	tBu
CHO	Ph
SO_3H	Et
SO_2NHMe	nPr
OH	Ph
COMe	Cl
COOH	Cl
$CONH_2$	Cl
CONHMe	Et
CONHMs	nPr
NHMs	Ph
NO_2	Me
OH	Et
COMe	nPr
COOH	Ph

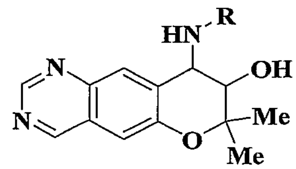
R^{13}	R^{14}
OMe	H
OEt	H
OiPr	H
OnPr	H
OBn	H
OPh	H
SMe	H
SEt	H
SiPr	H
SnPr	H
OCH_2CH_2Ph	H
SCH_2CH_2Ph	H
H	OMe
H	OEt
Cl	OiPr
Me	OnPr
Et	OBn
nPr	OPh
Ph	SMe
Me	SEt
Et	SiPr
nPr	SnPr
Ph	OCH_2CH_2Ph
NO_2	SCOMe
CHO	OMe
SO_3H	OEt
Cl	OnPr
Br	SMe
CH_2OH	SEt
CH_2NH_2	SiPr
F	SPh



R^{13}	R^{14}	R^{13}	R^{14}	R^{13}	R^{14}
H	Me	NO_2	H	OMe	H
H	Et	CHO	H	OEt	H
H	iPr	SO_3H	H	OiPr	H
H	nPr	Cl	H	OnPr	H
H	nBu	Br	H	OBn	H
H	tBu	CH_2OH	H	OPh	H
H	Ph	CH_2NH_2	H	SMe	H
Me	H	CH_2NHMe	H	SEt	H
Et	H	CH_2Ph	H	SiPr	H
iPr	H	COMe	H	SnPr	H
nPr	H	COOH	H	OCH_2CH_2Ph	H
nBu	H	$CONH_2$	H	SCH_2CH_2Ph	H
tBu	H	CONHMe	Et	H	OMe
Ph	NO_2	CONHMs	iPr	H	OEt
H	CHO	NHMs	nPr	Cl	OiPr
H	SO_3H	NHCOMe	nBu	Me	OnPr
H	Cl	NO_2	tBu	Et	OBn
H	Br	CHO	Ph	nPr	OPh
H	CH_2OH	SO_3H	Et	Ph	SMe
H	CH_2NH_2	SO_2NHMe	nPr	Me	SEt
Cl	CH_2NHMe	OH	Ph	Et	SiPr
Cl	CH_2Ph	COMe	Cl	nPr	SnPr
Cl	COMe	COOH	Cl	Ph	OCH_2CH_2Ph
Et	COOH	$CONH_2$	Cl	NO_2	SCOMe
nPr	$CONH_2$	CONHMe	Et	CHO	OMe
Ph	CONHMe	CONHMs	nPr	SO_3H	OEt
H	CONHMs	NHMs	Ph	Cl	OnPr
H	NHMs	NO_2	Me	Br	SMe
H	NHCOMe	OH	Et	CH_2OH	SEt
Me	CO_2H	COMe	nPr	CH_2NH_2	SiPr
Et	H	COOH	Ph	F	SPh



R^{13}	R^{14}	R^{13}	R^{14}	R^{13}	R^{14}
H	Me	NO_2	H	OMe	H
H	Et	CHO	H	OEt	H
H	iPr	SO_3H	H	OiPr	H
H	nPr	Cl	H	OnPr	H
H	nBu	Br	H	OBn	H
H	tBu	CH_2OH	H	OPh	H
H	Ph	CH_2NH_2	H	SMe	H
Me	H	CH_2NHMe	H	SEt	H
Et	H	CH_2Ph	H	SiPr	H
iPr	H	COMe	H	SnPr	H
nPr	H	COOH	H	OCH_2CH_2Ph	H
nBu	H	$CONH_2$	H	SCH_2CH_2Ph	H
tBu	H	CONHMe	Et	H	OMe
Ph	NO_2	CONHMs	iPr	H	OEt
H	CHO	NHMs	nPr	Cl	OiPr
H	SO_3H	NHCOMe	nBu	Me	OnPr
H	Cl	NO_2	tBu	Et	OBn
H	Br	CHO	Ph	nPr	OPh
H	CH_2OH	SO_3H	Et	Ph	SMe
H	CH_2NH_2	SO_2NHMe	nPr	Me	SEt
Cl	CH_2NHMe	OH	Ph	Et	SiPr
Cl	CH_2Ph	COMe	Cl	nPr	SnPr
Cl	COMe	COOH	Cl	Ph	OCH_2CH_2Ph
Et	COOH	$CONH_2$	Cl	NO_2	SCOMe
nPr	$CONH_2$	CONHMe	Et	CHO	OMe
Ph	CONHMe	CONHMs	nPr	SO_3H	OEt
H	CONHMs	NHMs	Ph	Cl	OnPr
H	NHMs	NO_2	Me	Br	SMe
H	NHCOMe	OH	Et	CH_2OH	SEt
Me	CO_2H	COMe	nPr	CH_2NH_2	SiPr
Et	H	COOH	Ph	F	SPh



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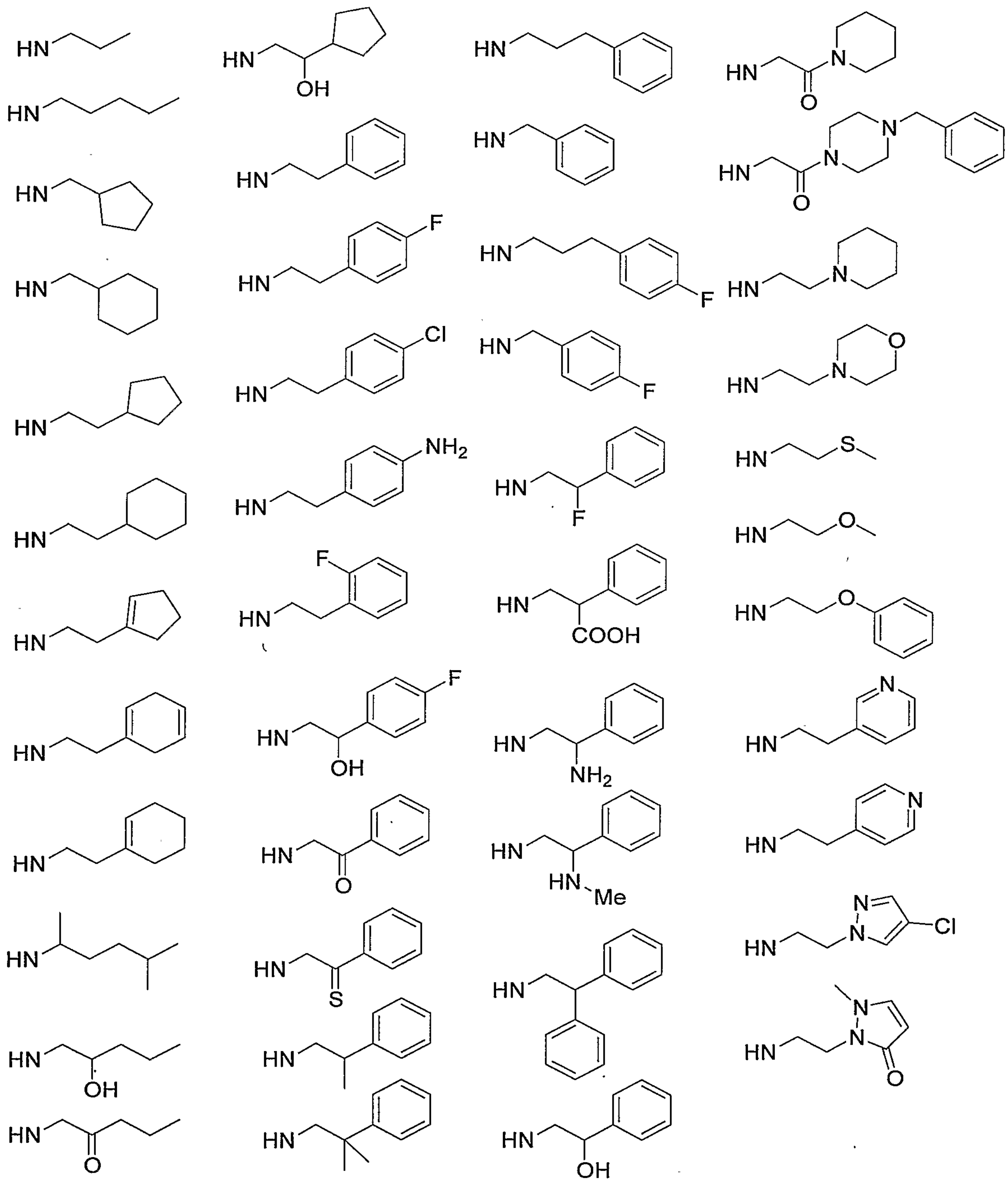
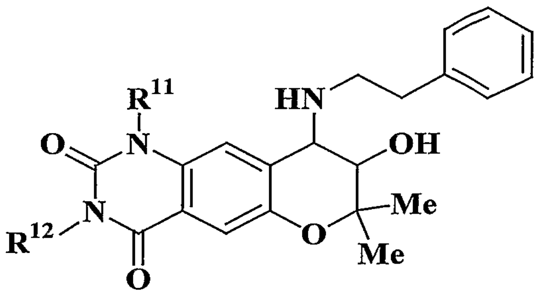
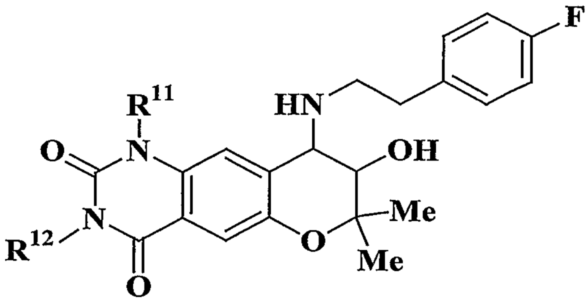
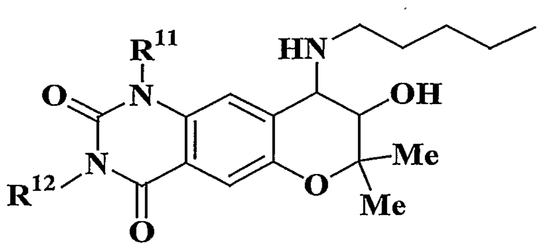




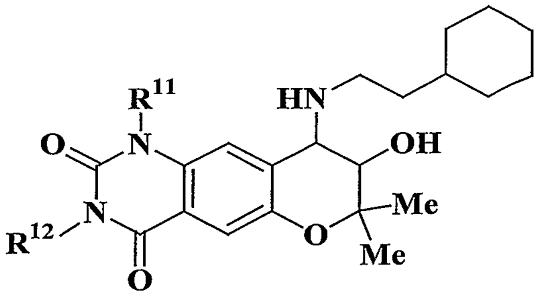
R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



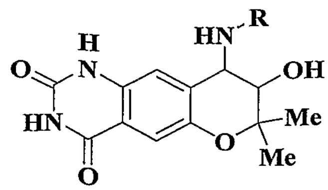
R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



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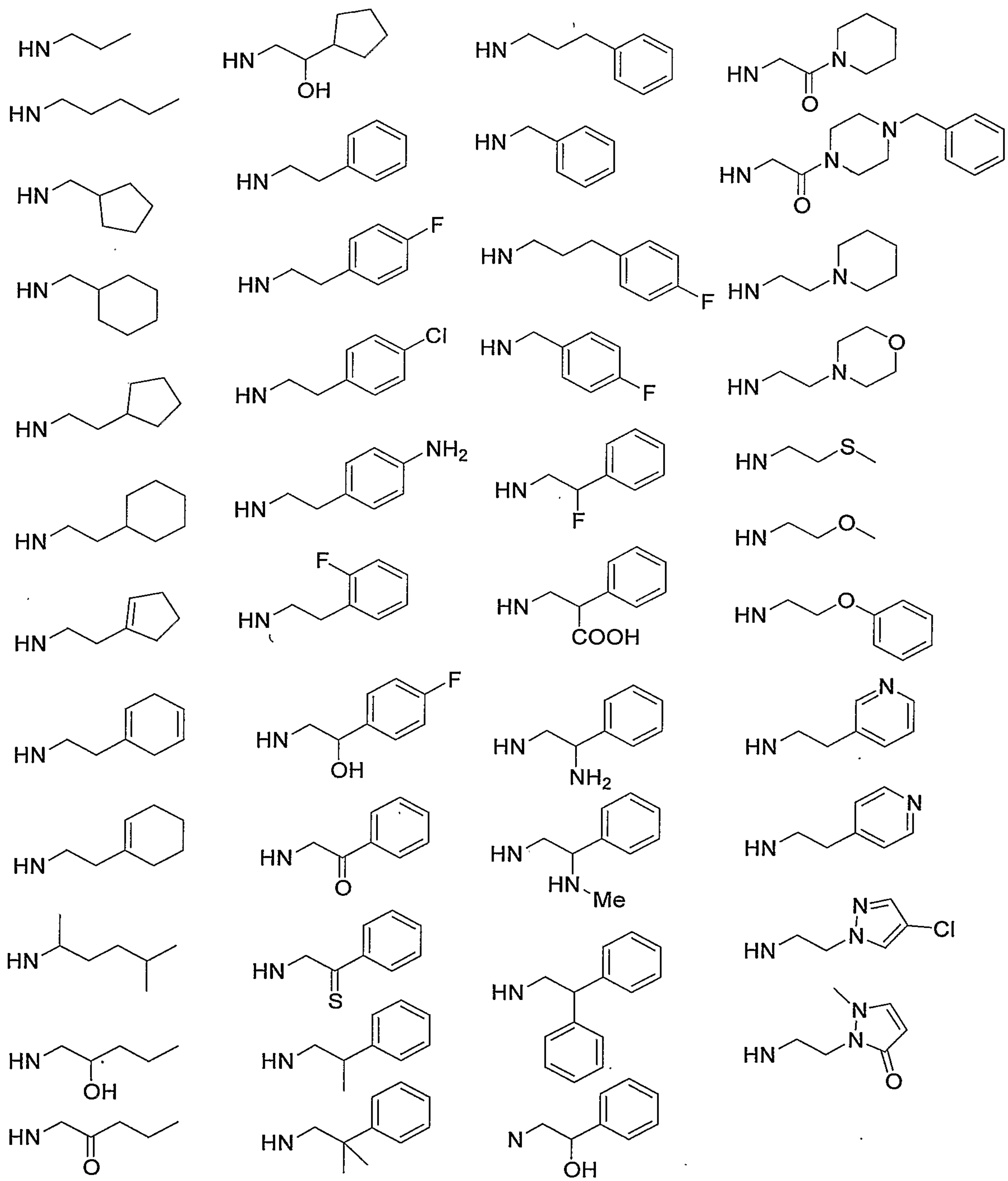
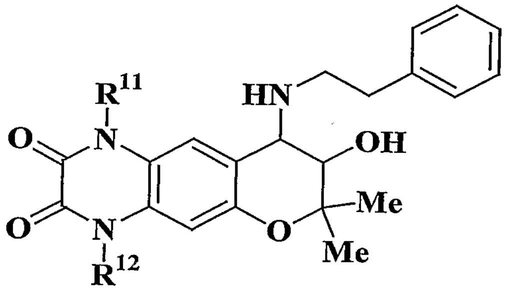
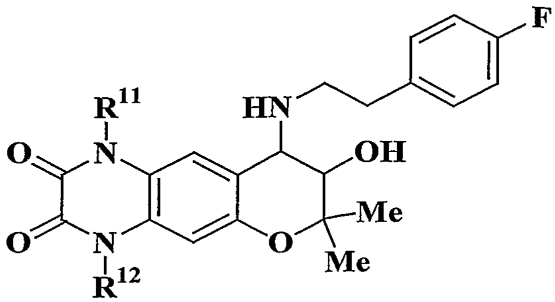
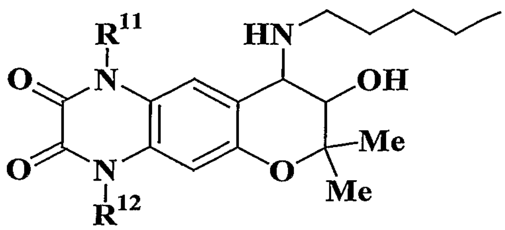




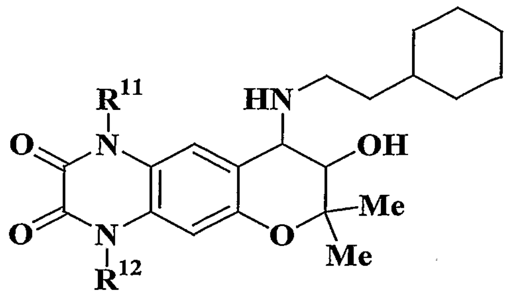
R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



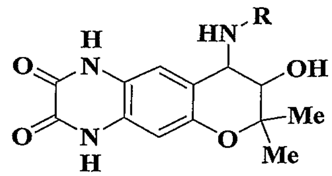
R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



R^{11}	R^{12}
H	Me
H	Et
H	iPr
H	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH_2OH
Me	CH_2OMe
Me	CH_2NH_2
Me	Me
Et	CH_2NH_2
Et	CH_2NHMe
Et	CH_2Ph
iPr	CH_2Ph
nPr	CH_2CH_2Ph
nBu	H
tBu	Me
Ph	H
CH_2OH	Me
CH_2OH	Et
CH_2OMe	nPr
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH_2NHMe	Et
CH_2Ph	nPr
CH_2Ph	Ph
CH_2CH_2Ph	CH_2Ph



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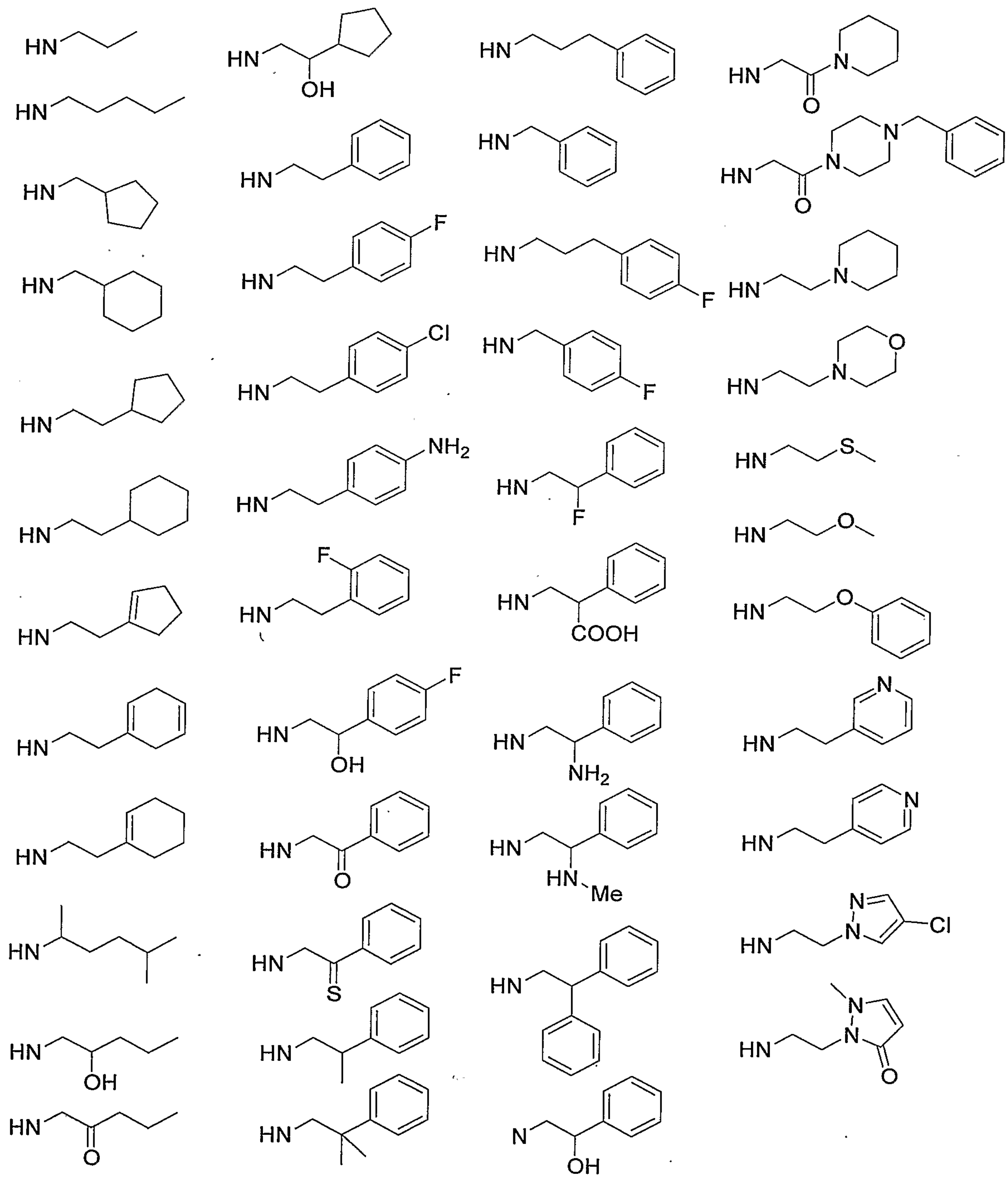
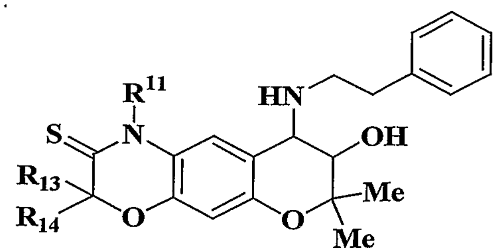
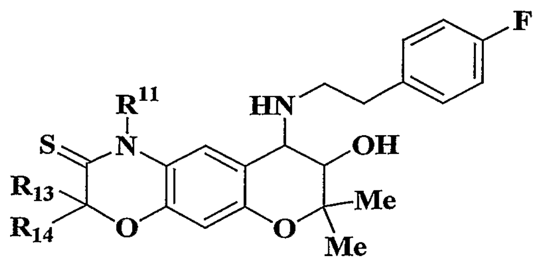




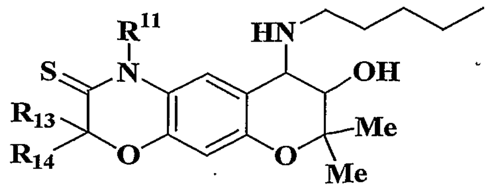
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	H
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



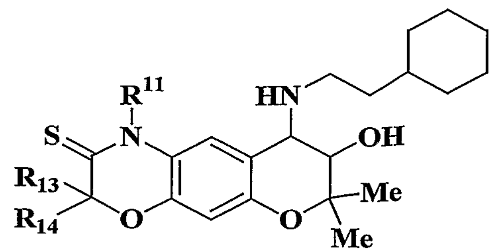
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



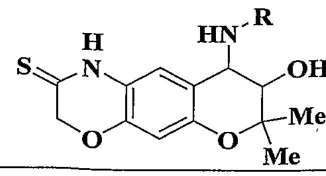
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	H
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

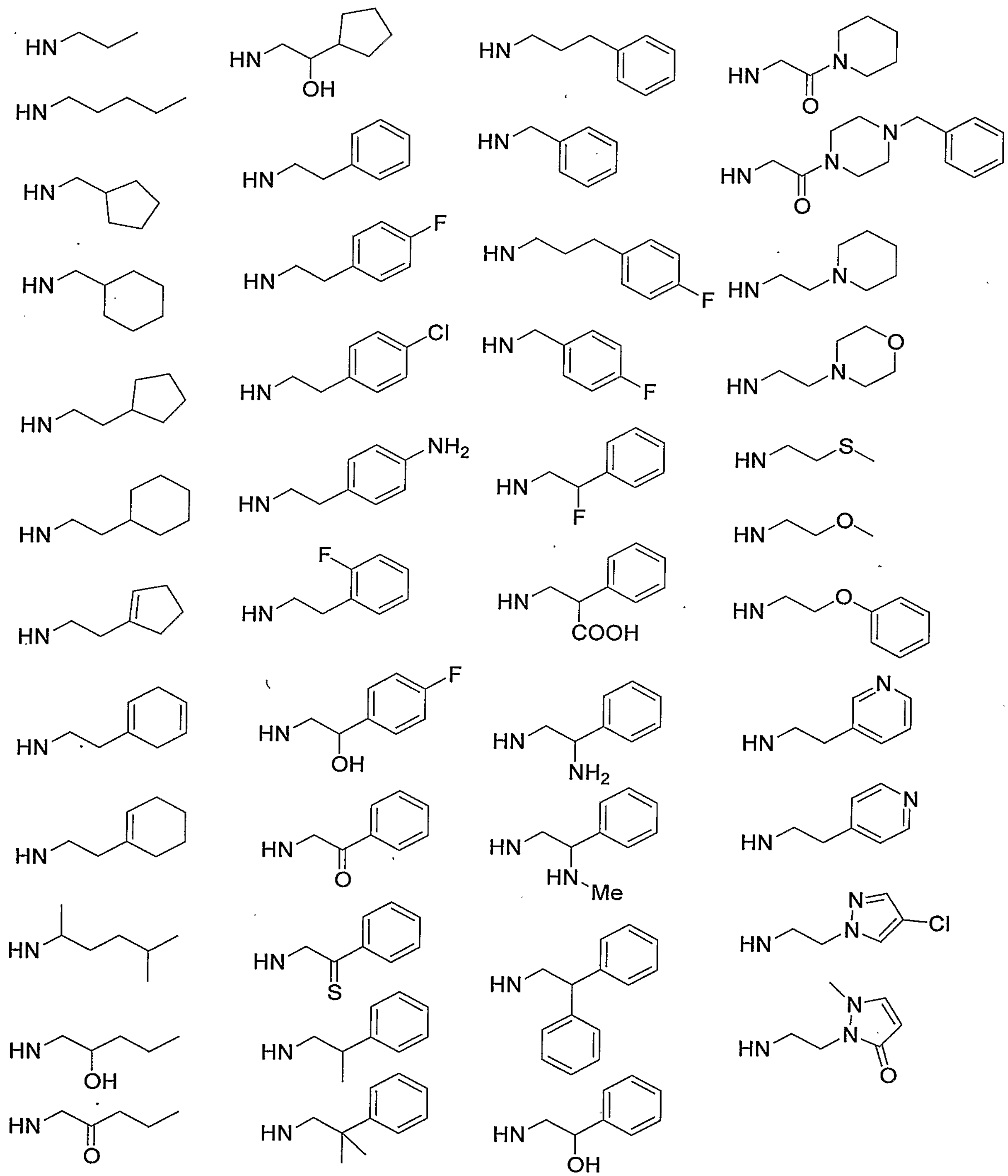
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H

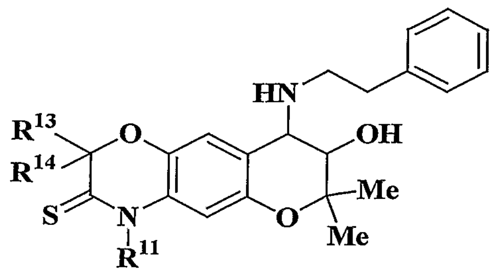


R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H

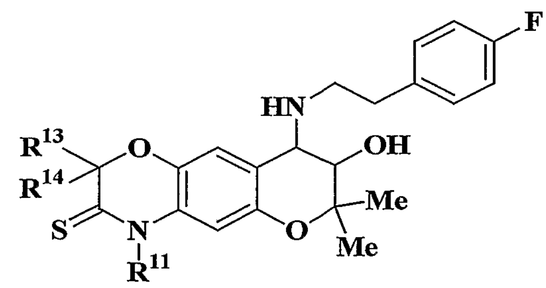


HN—R

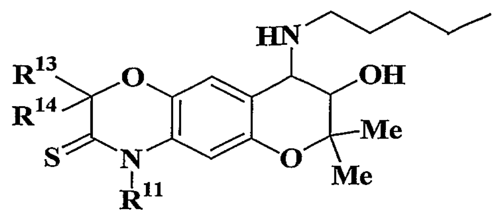




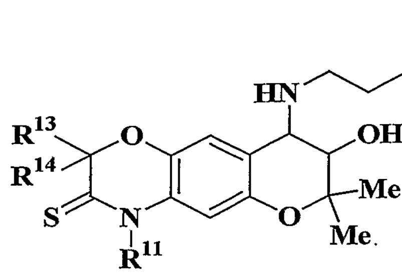
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



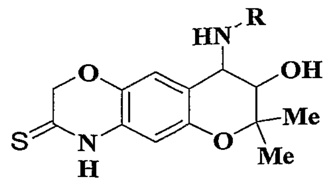
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



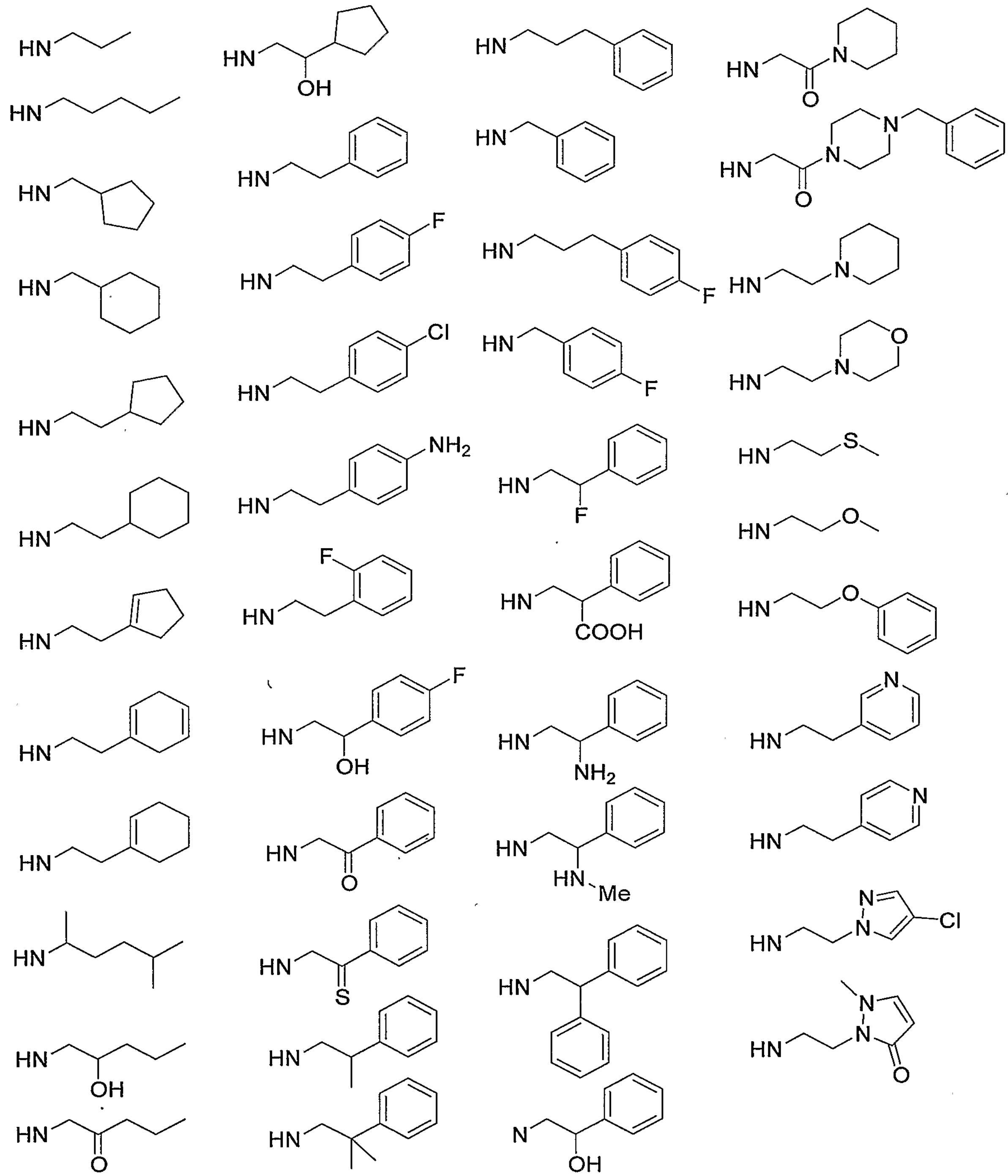
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	H
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

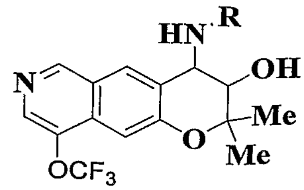
R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H

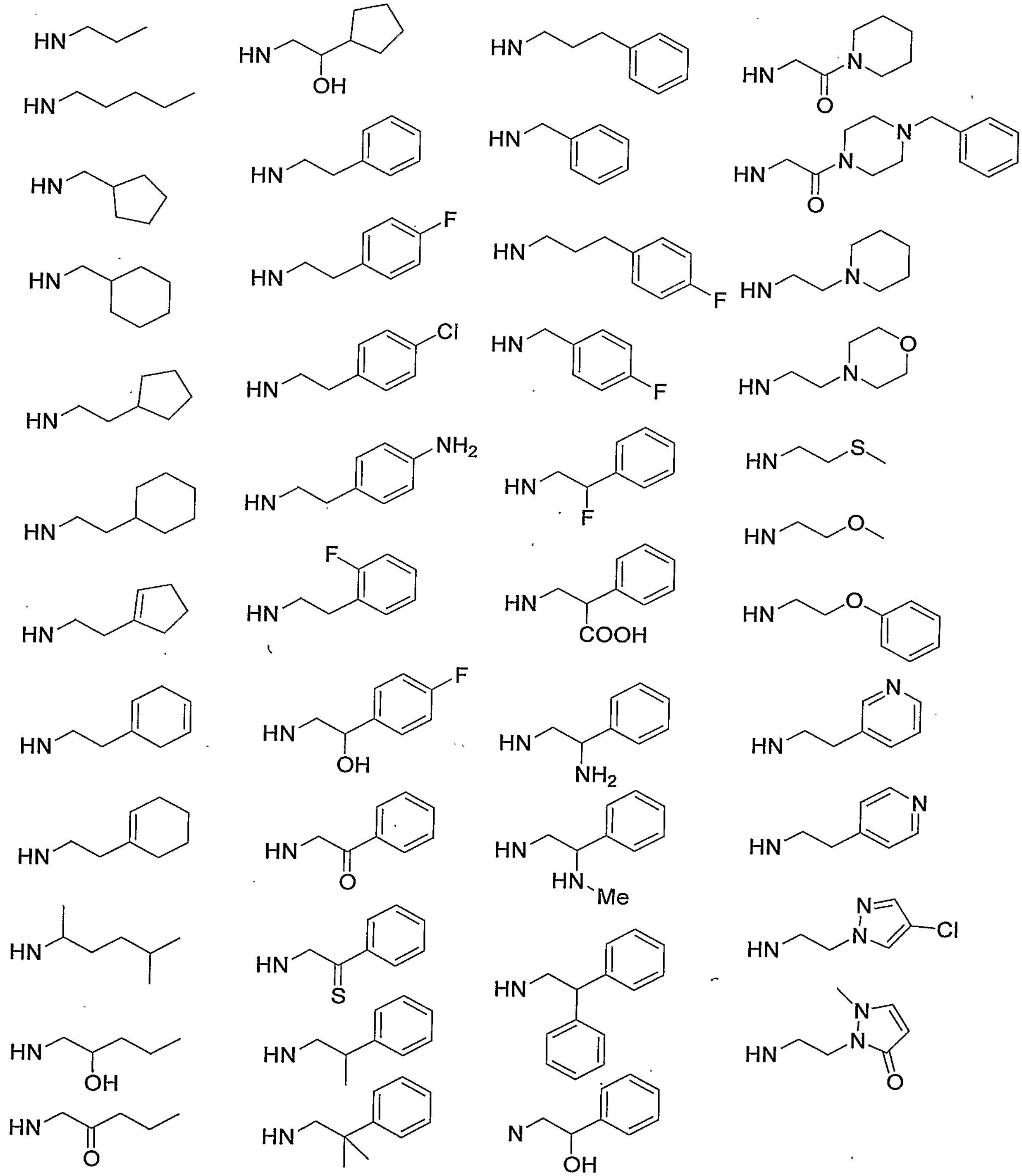


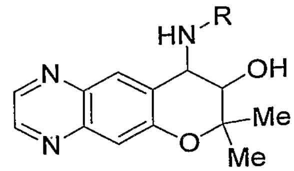
HN—R



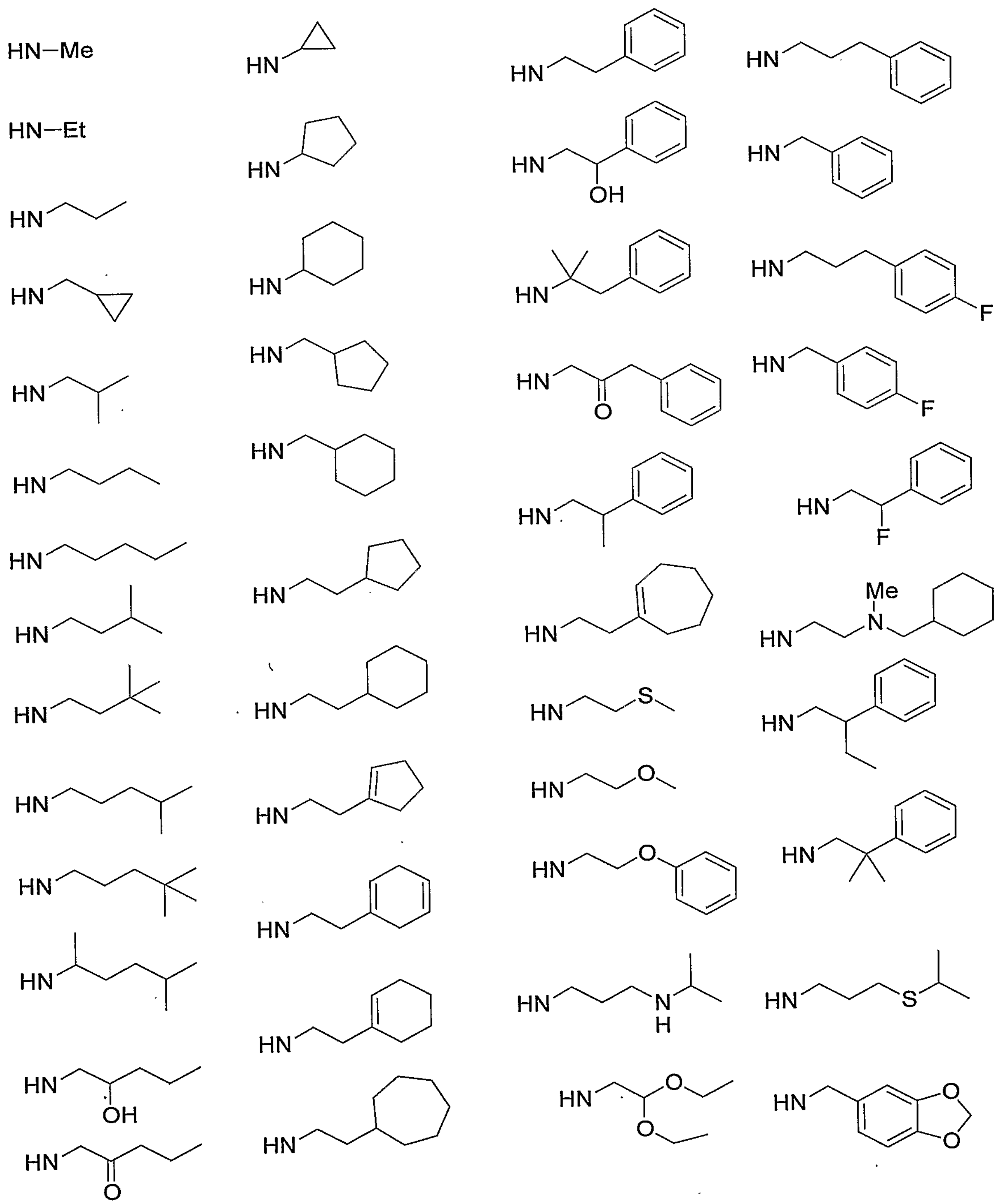


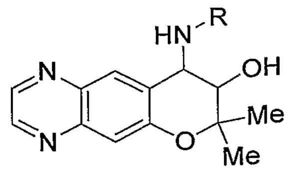
HN—R

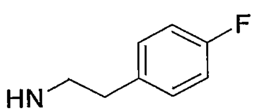
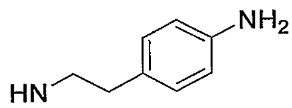
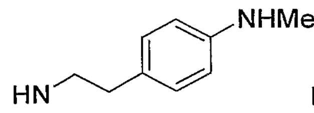
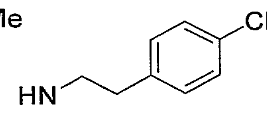
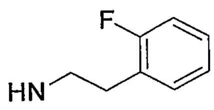
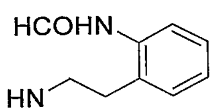
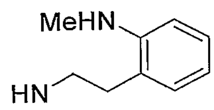
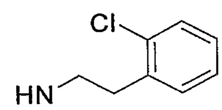
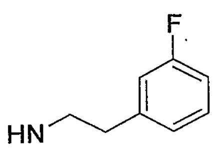
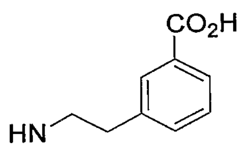
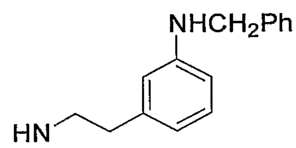
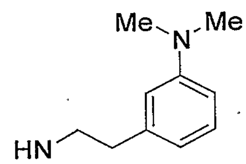
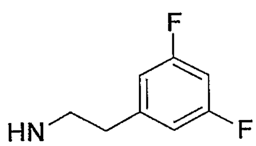
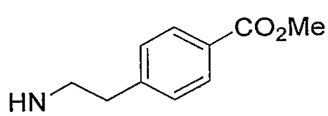
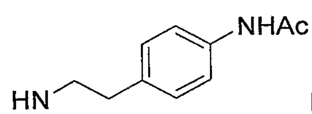
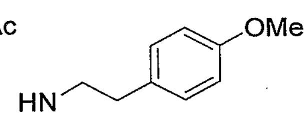
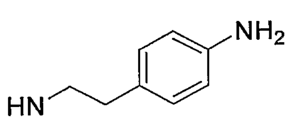
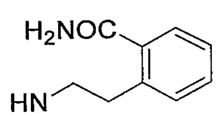
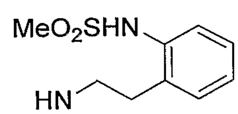
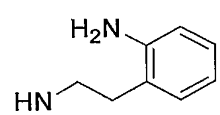
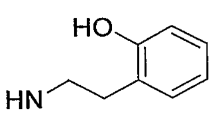
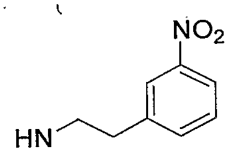
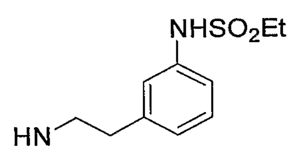
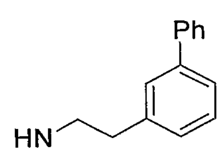
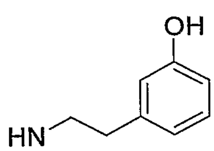
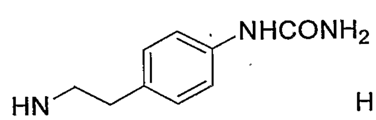
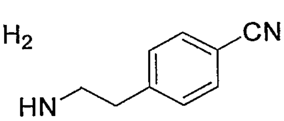
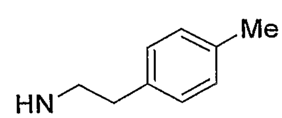
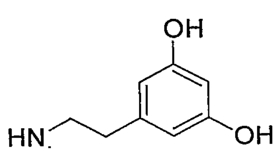
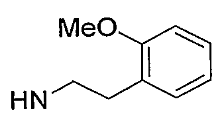
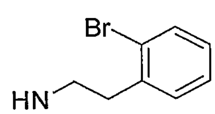
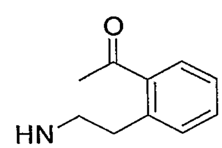
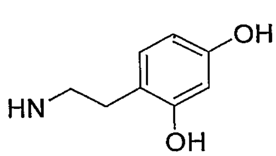
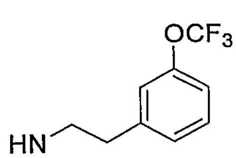
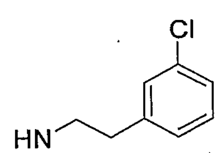
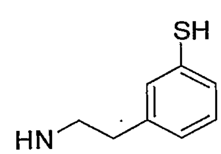


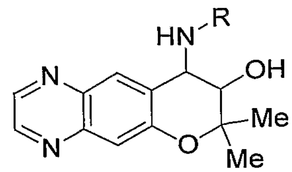


HN—R





HN−R			
			
			
			
			
			
			
			
			
			



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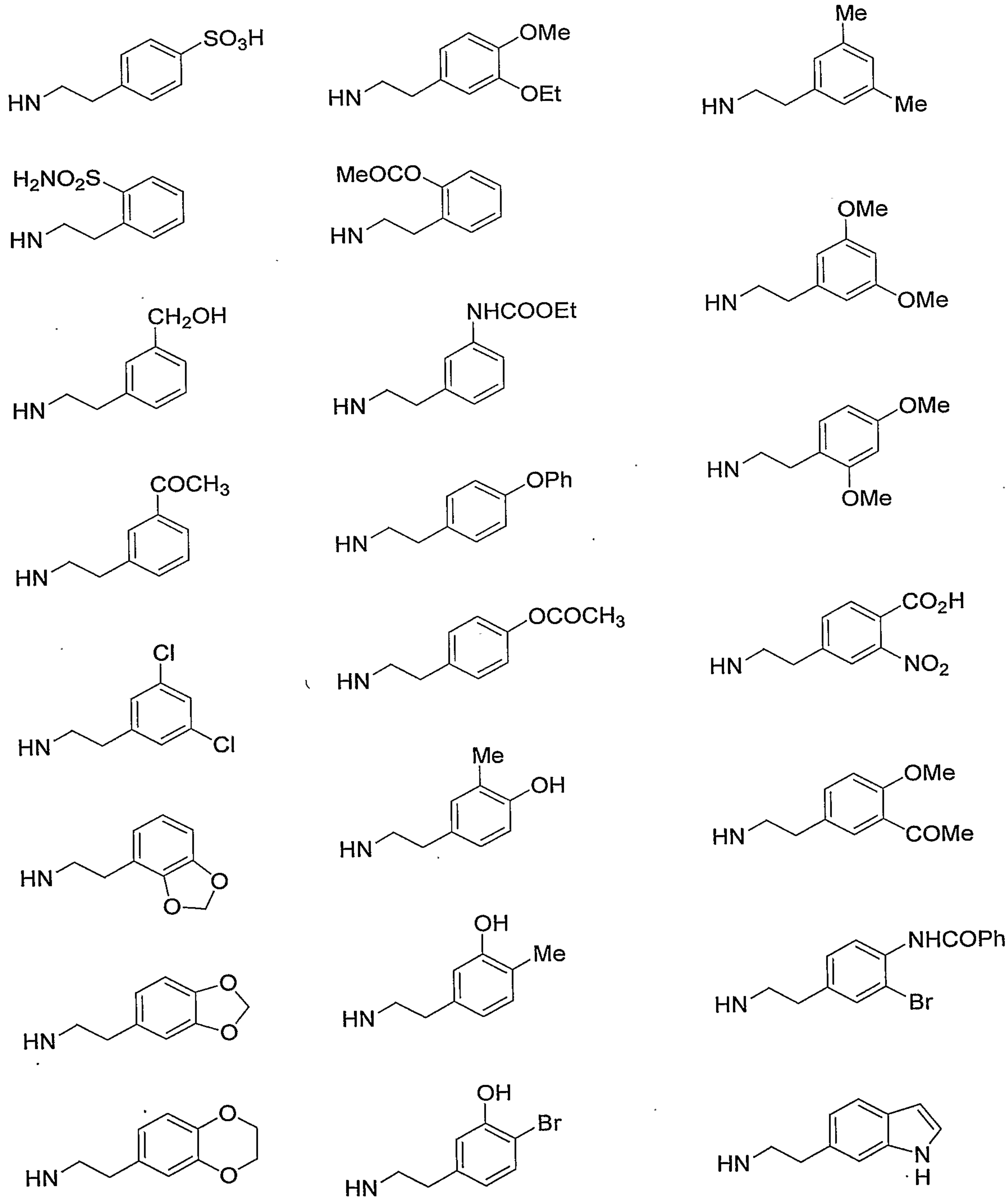

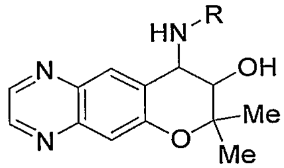

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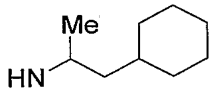	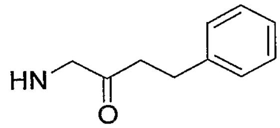	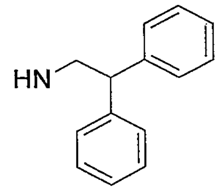
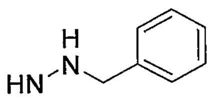	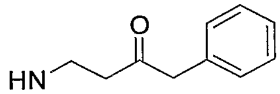	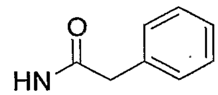
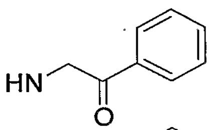	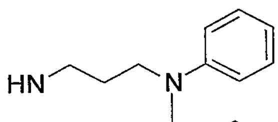	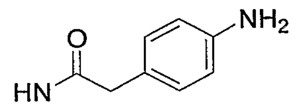
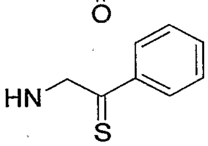	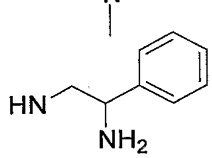	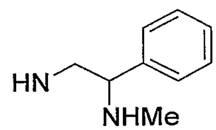
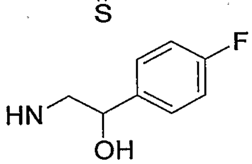	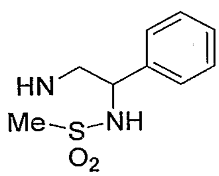	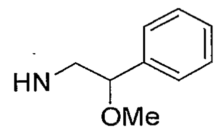
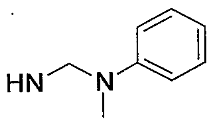	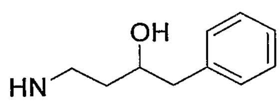	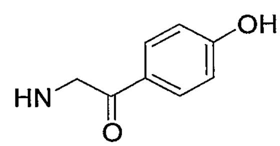
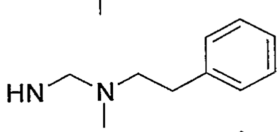	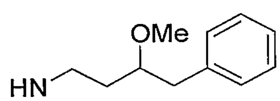	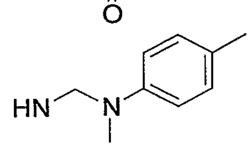
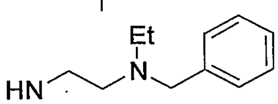	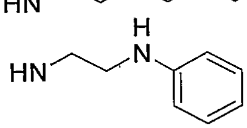	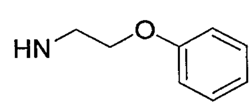
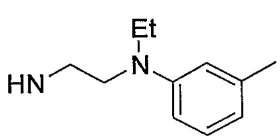	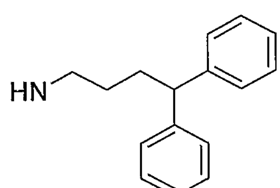	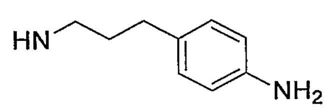
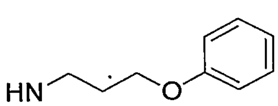	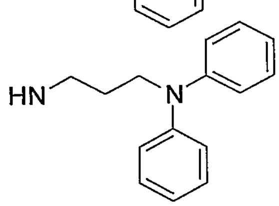	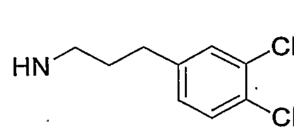
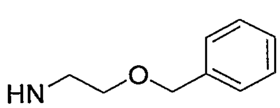		

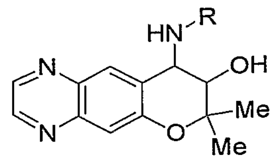

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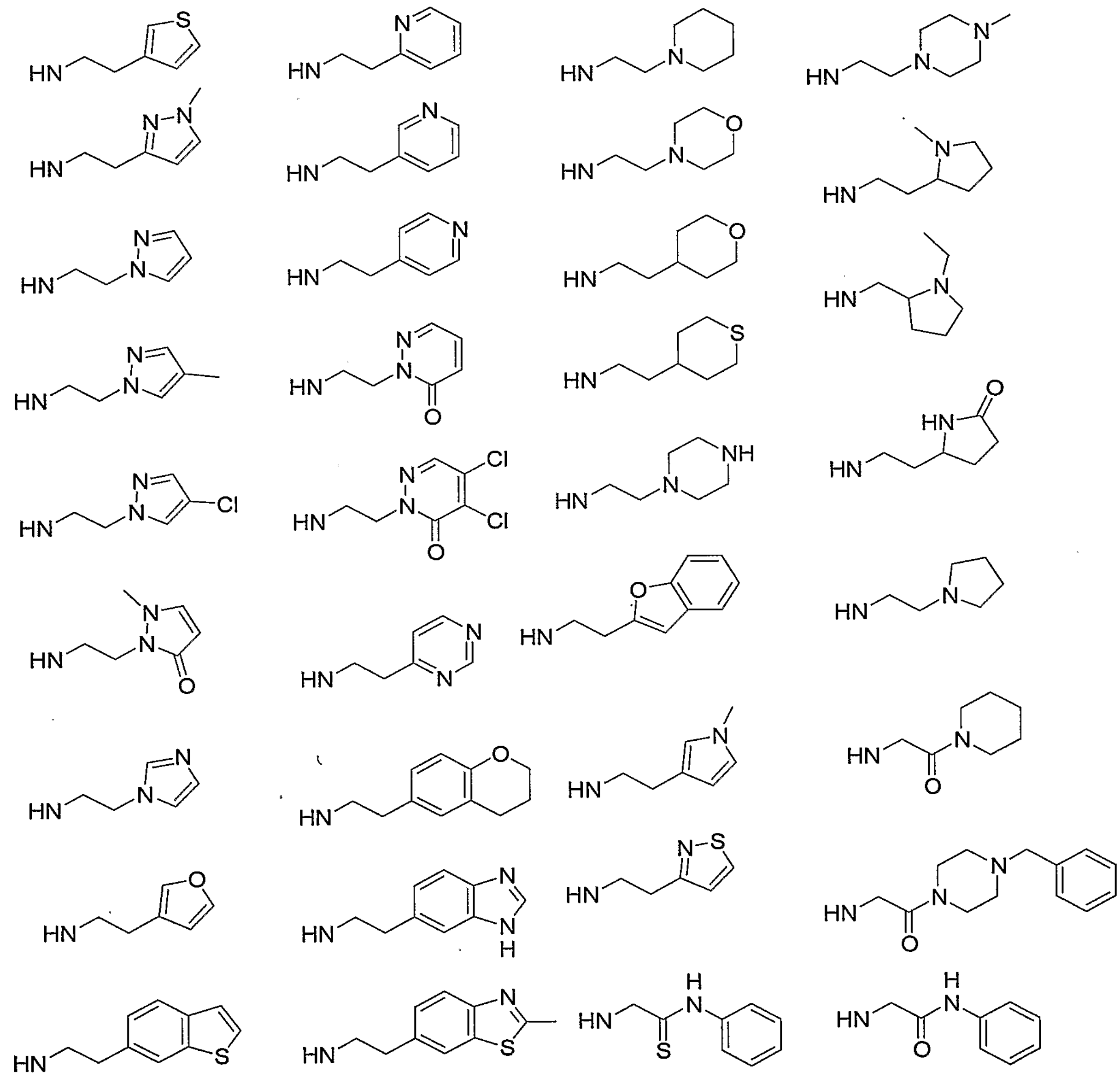

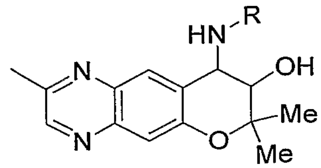

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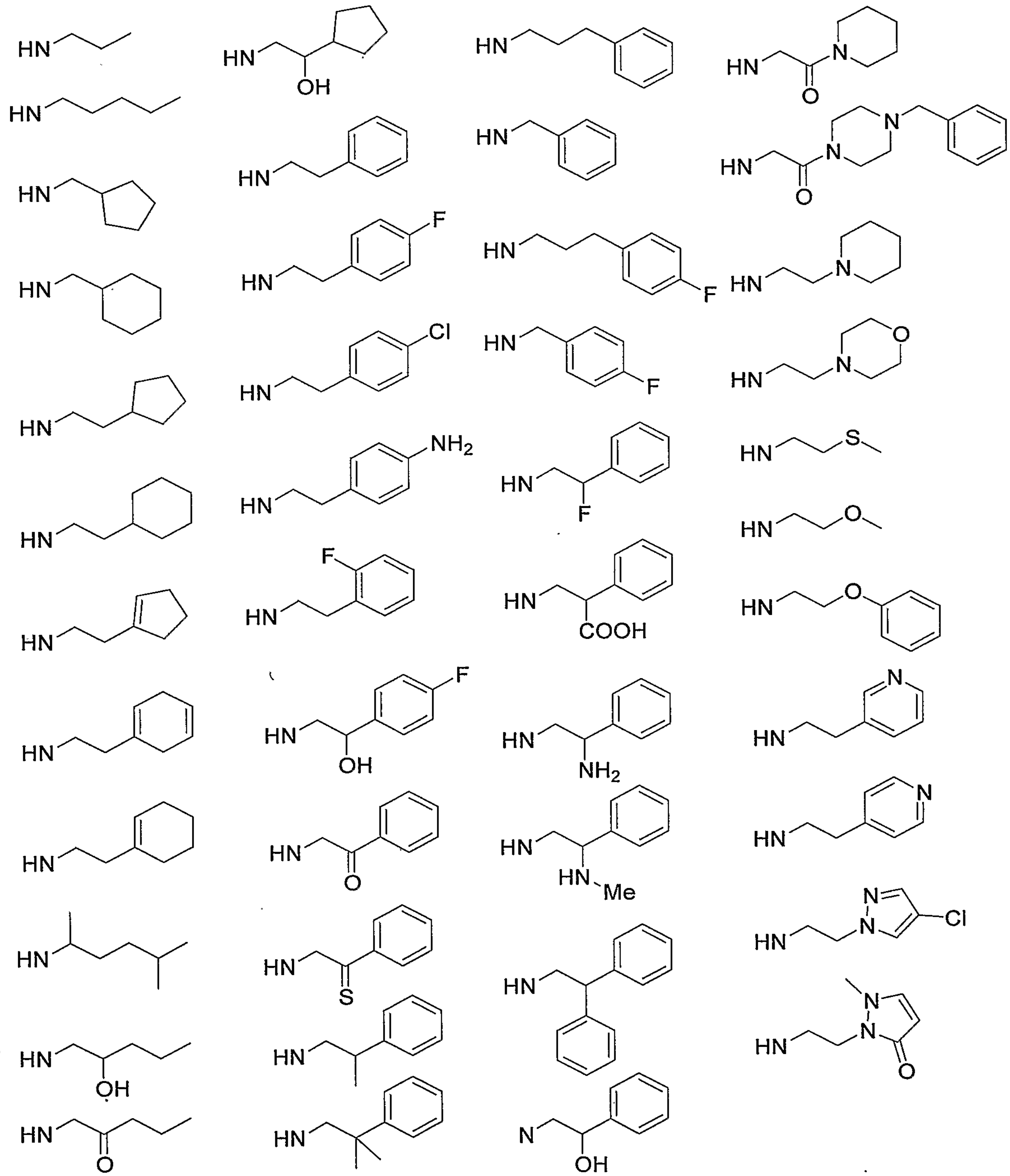

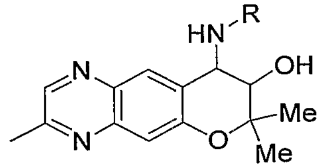

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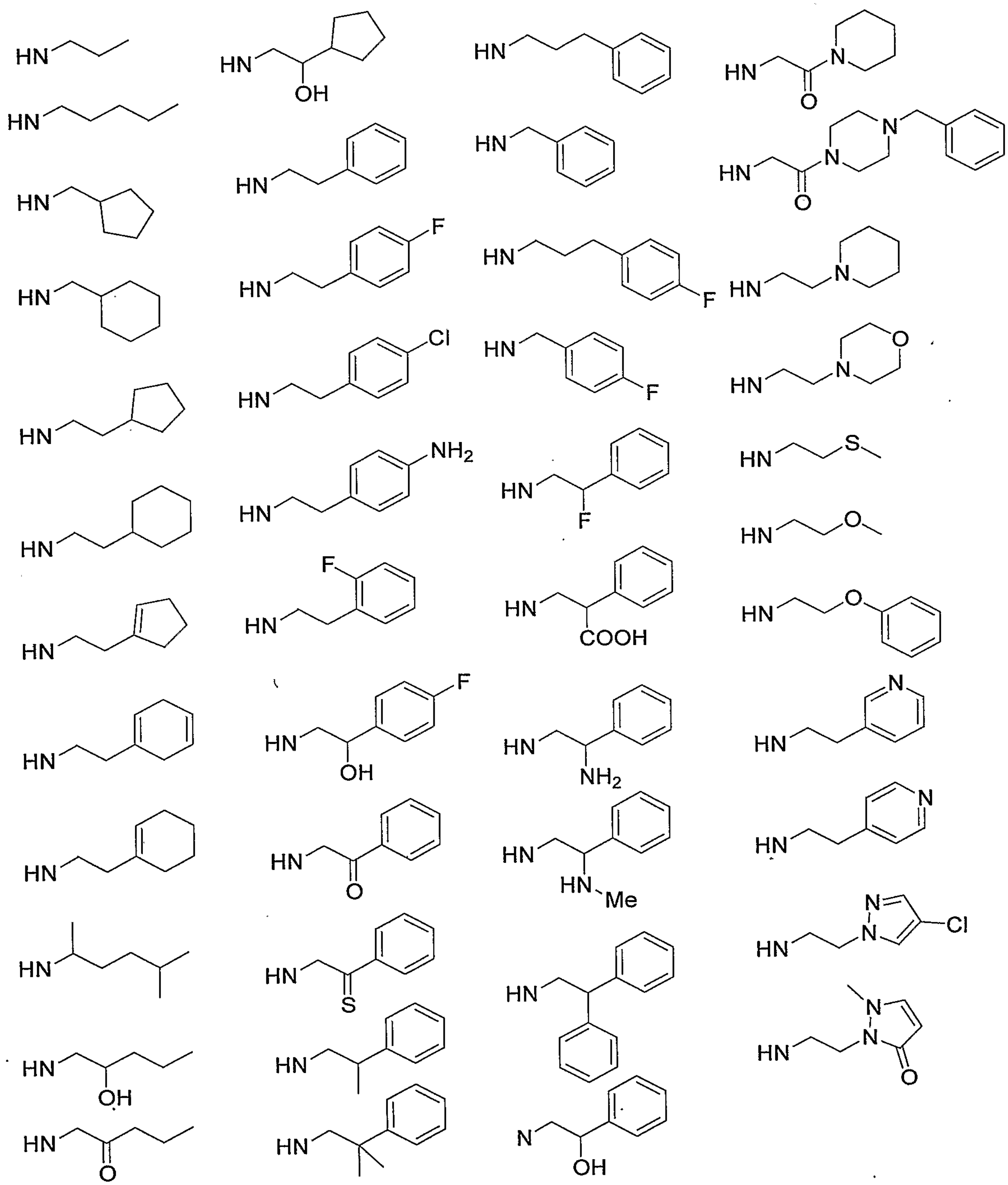

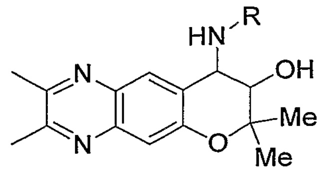

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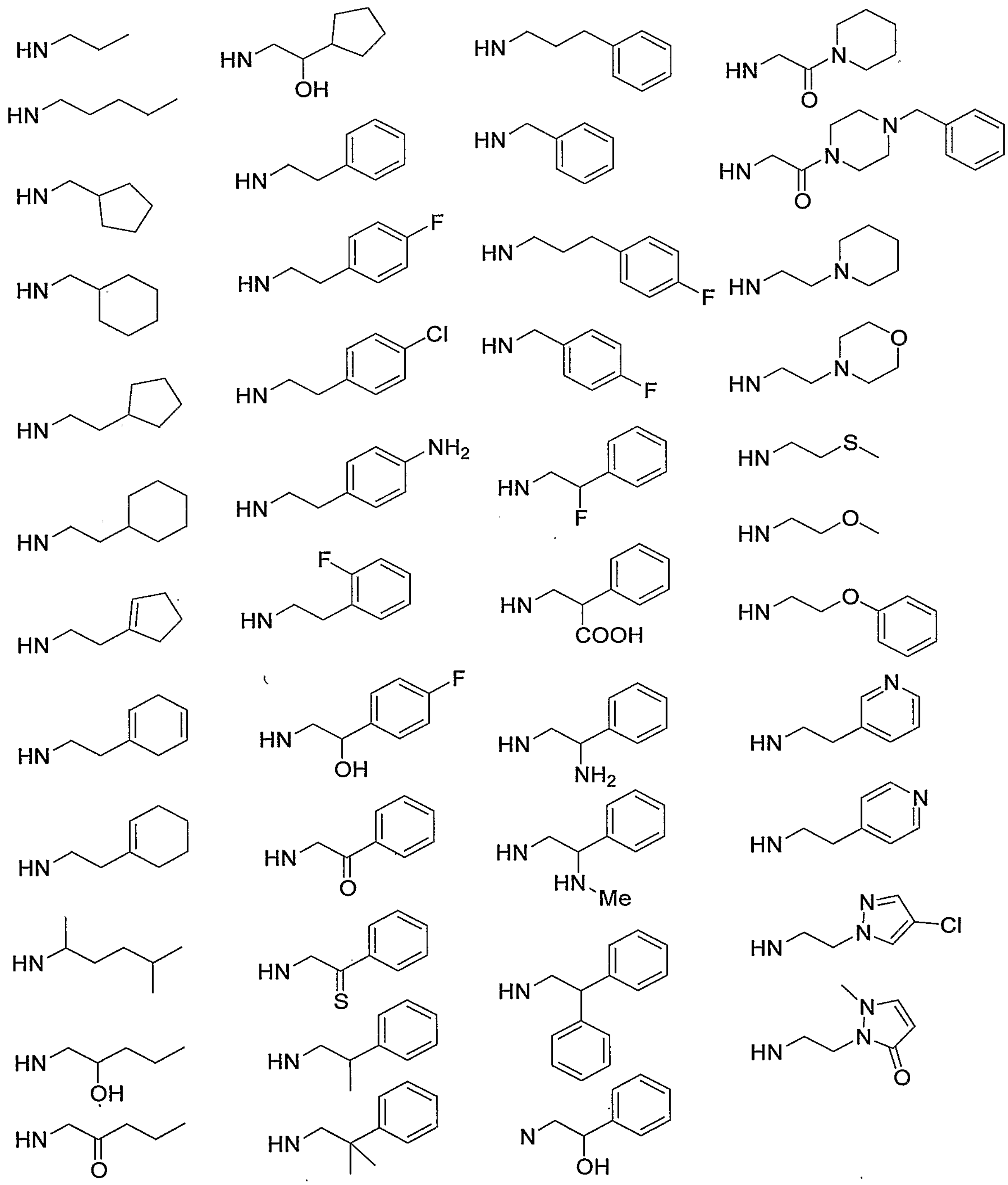

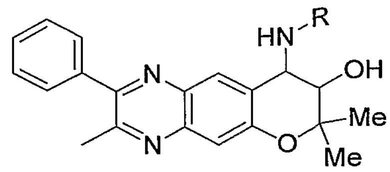

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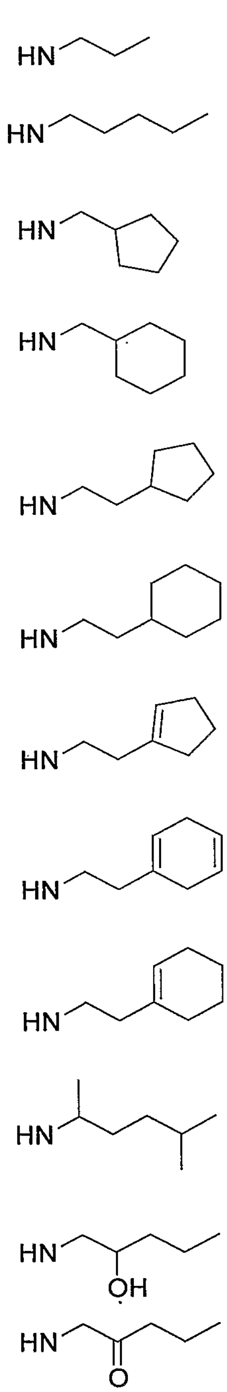

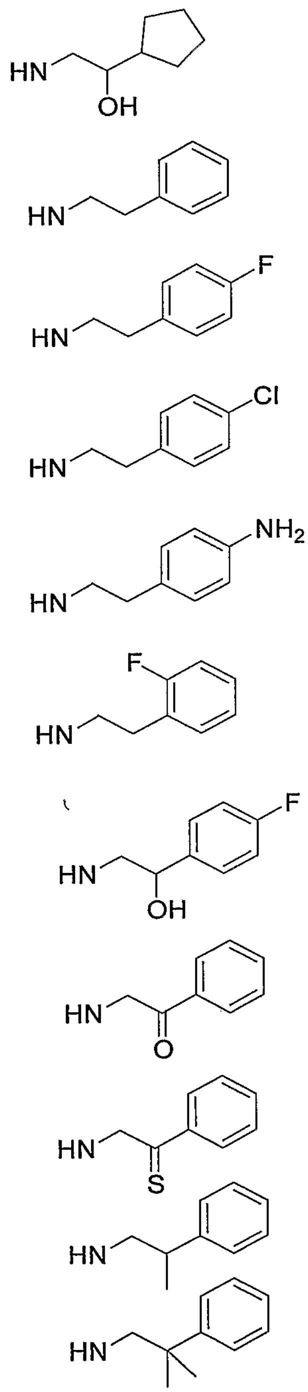

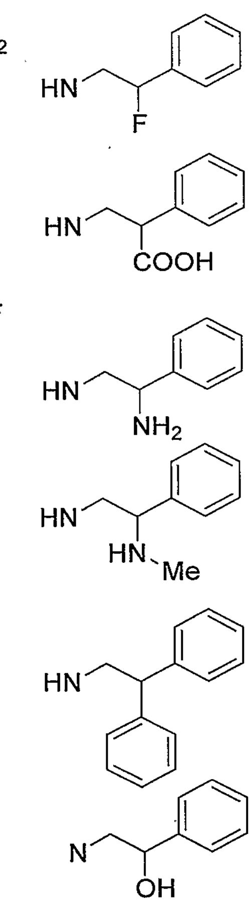

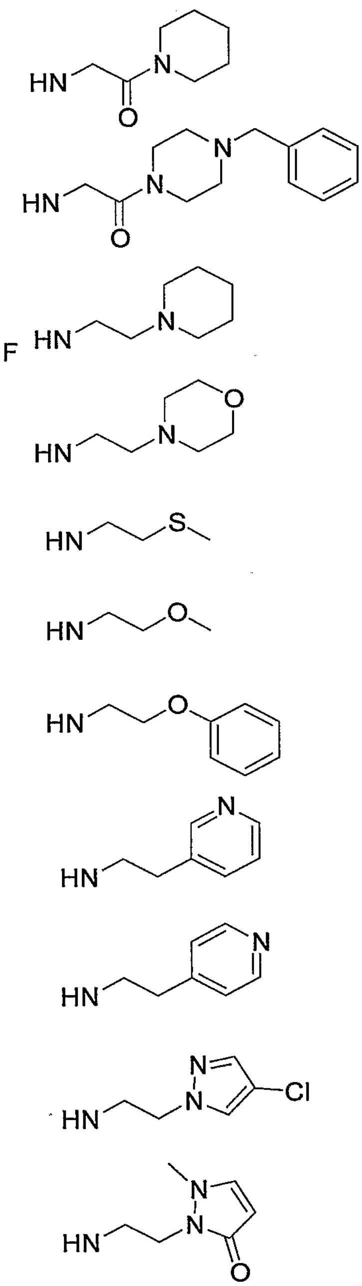

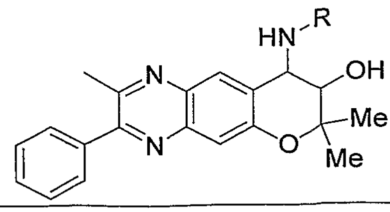

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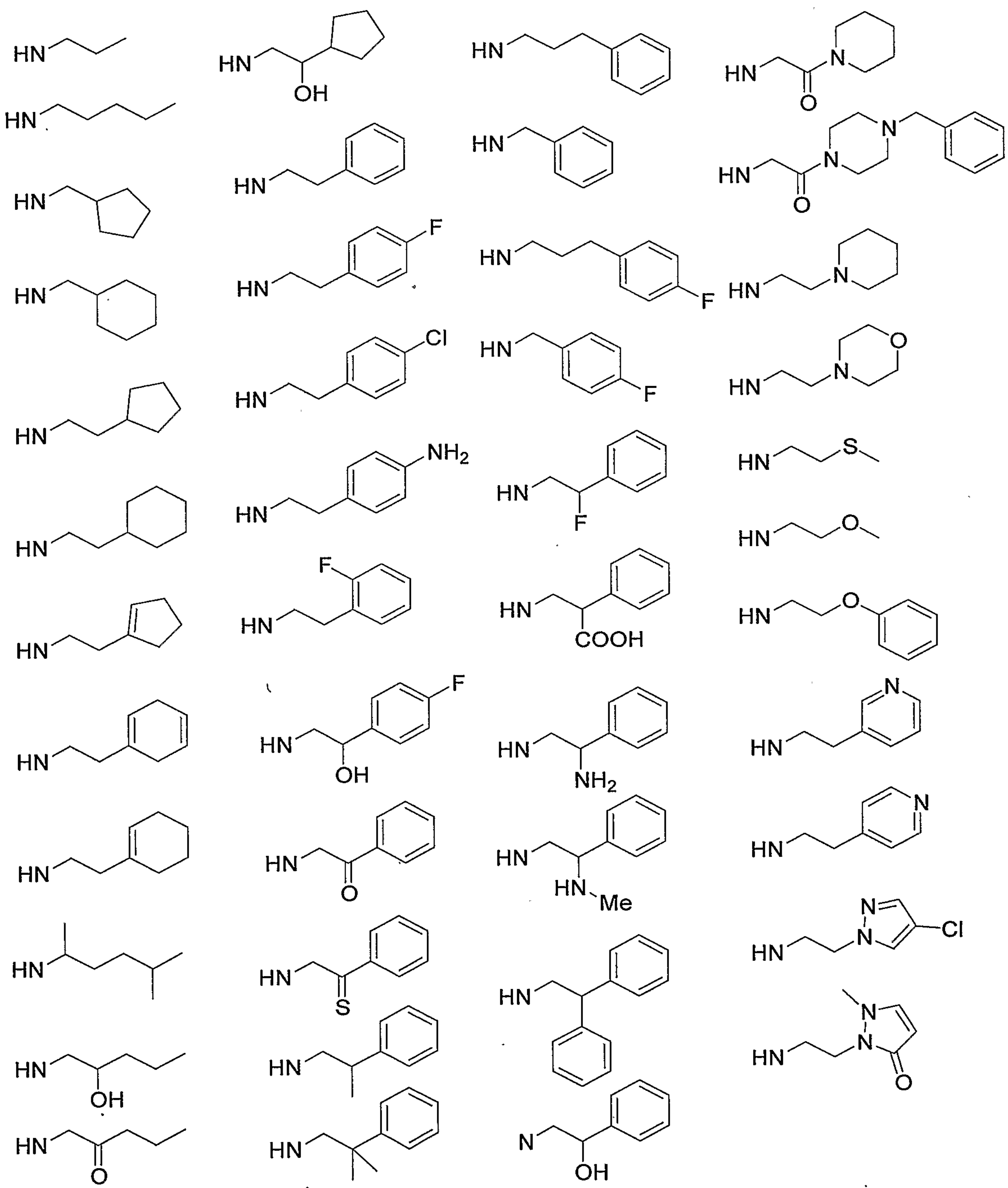

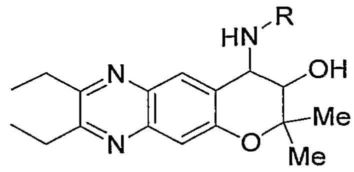

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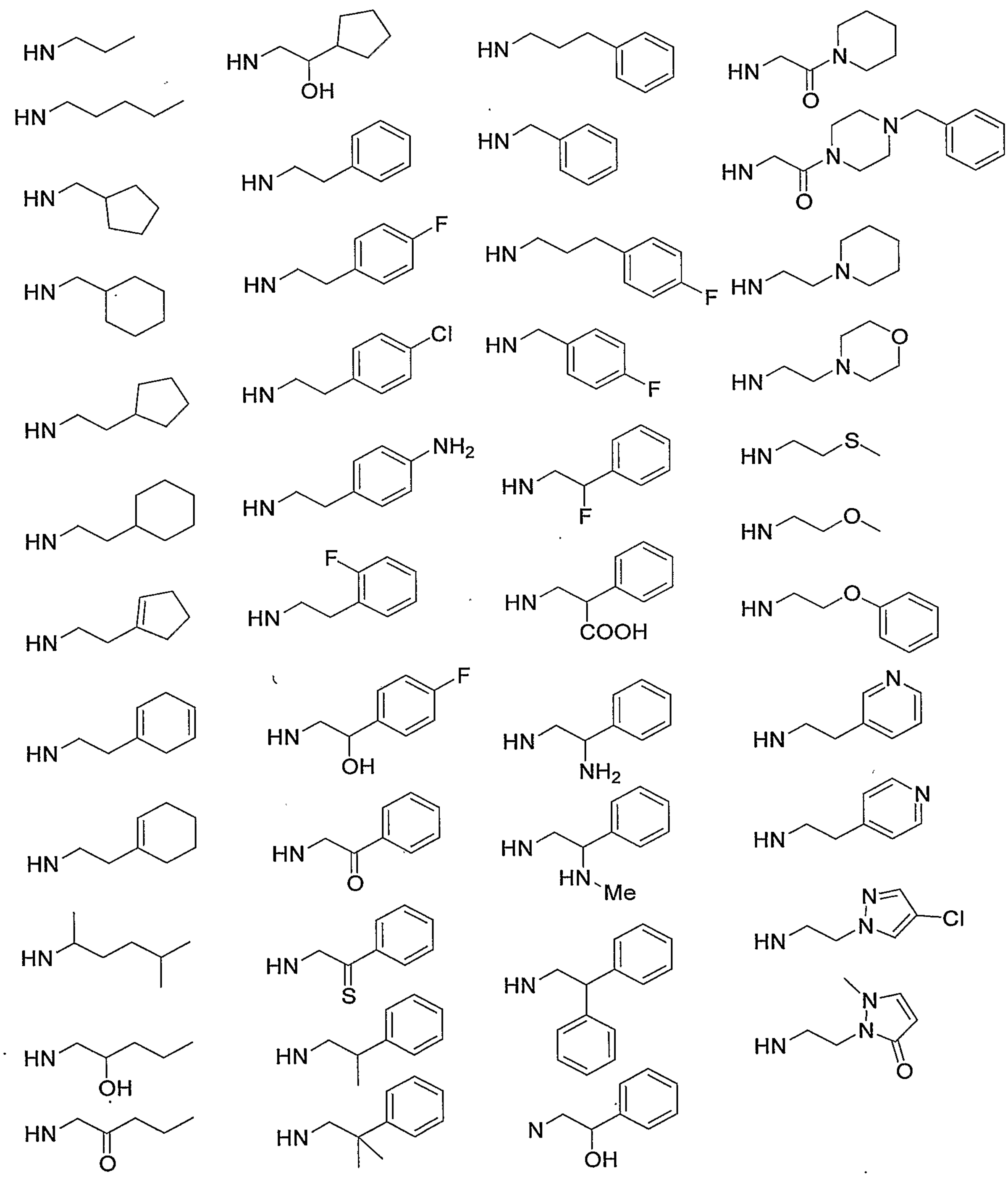

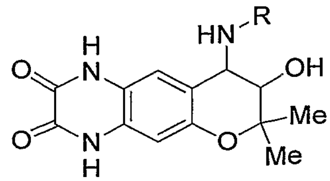

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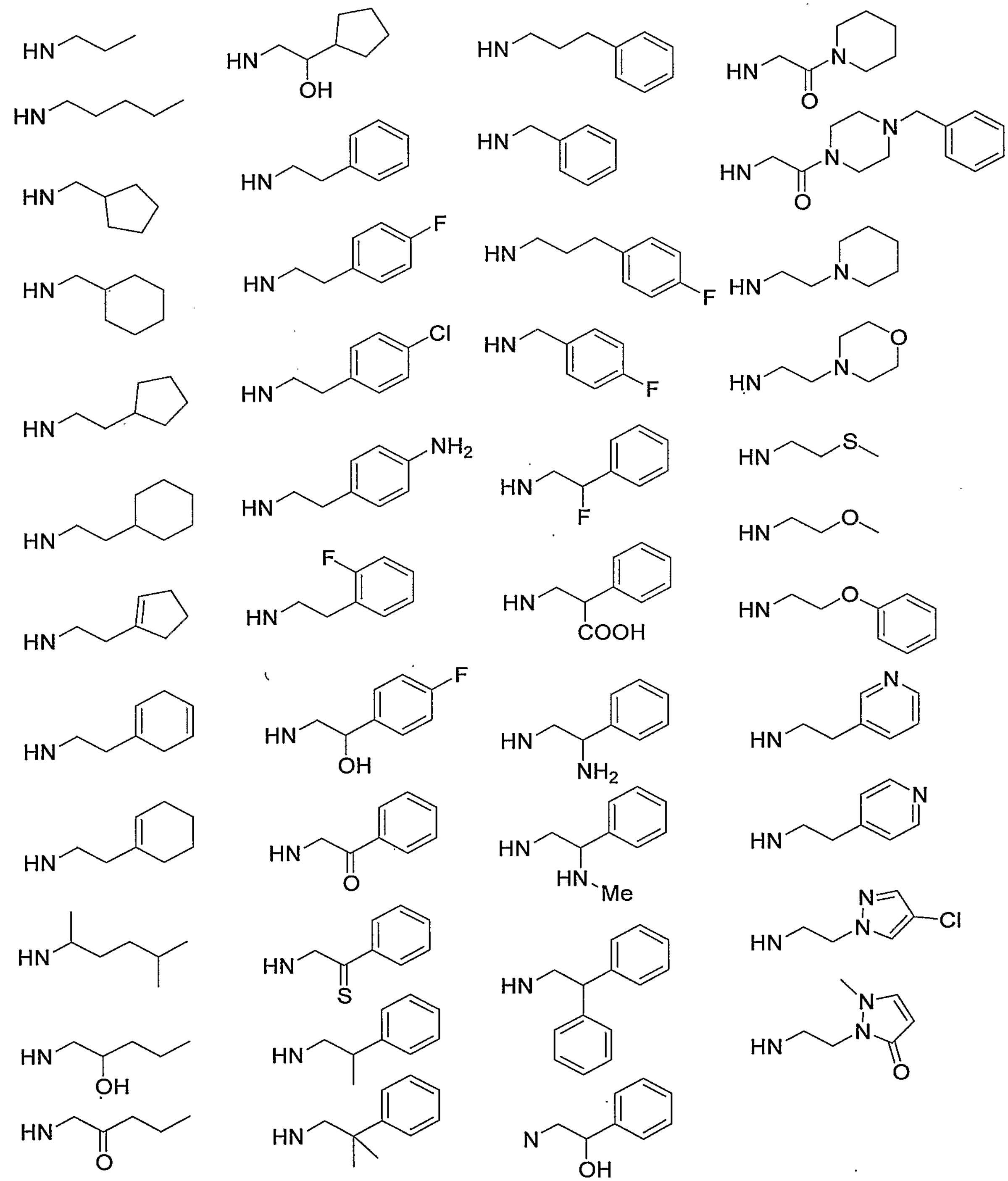

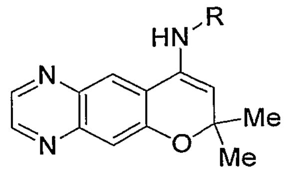

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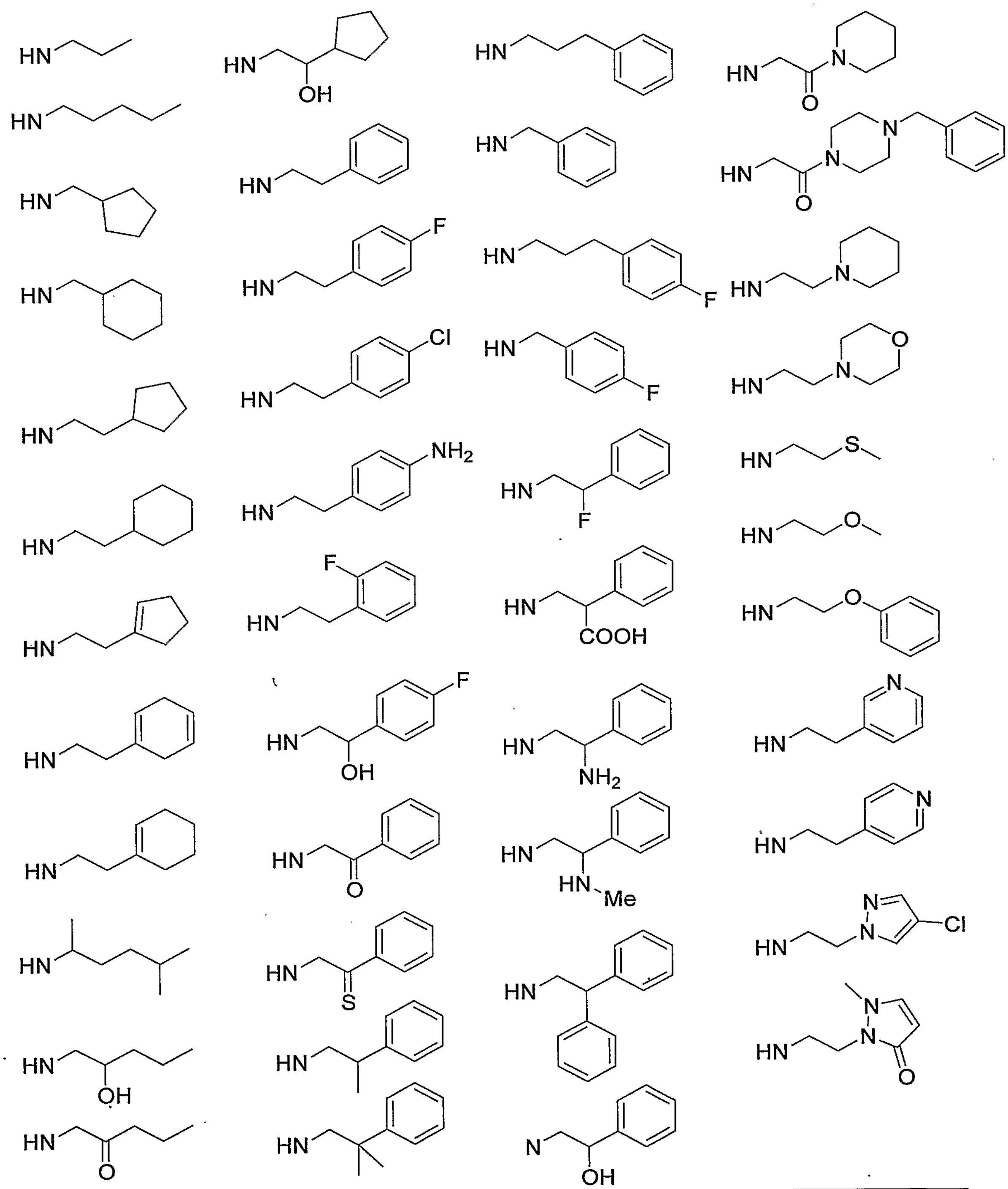

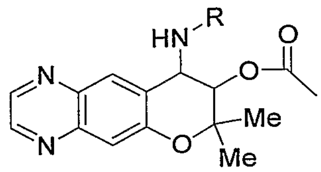

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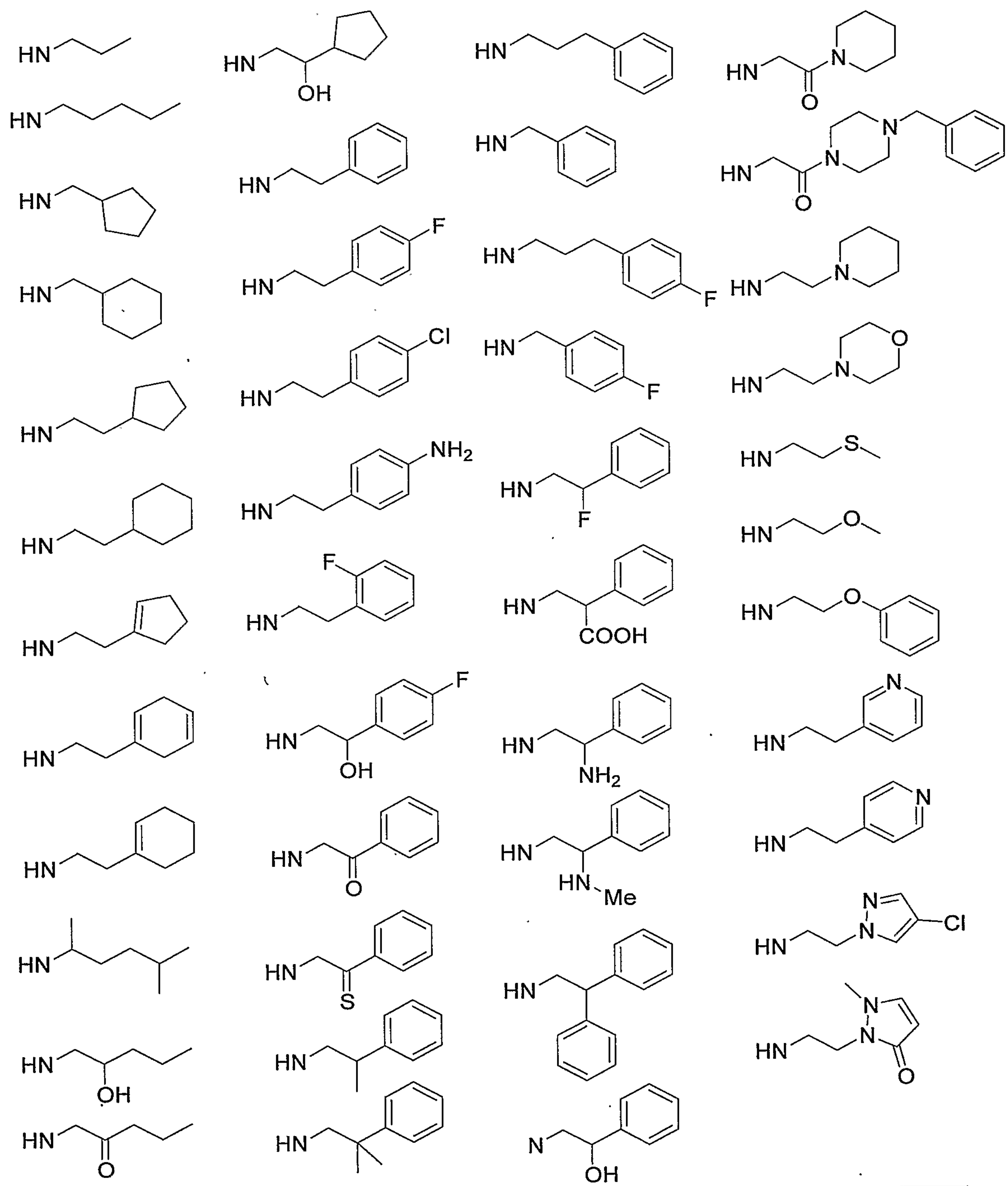

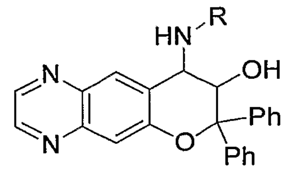

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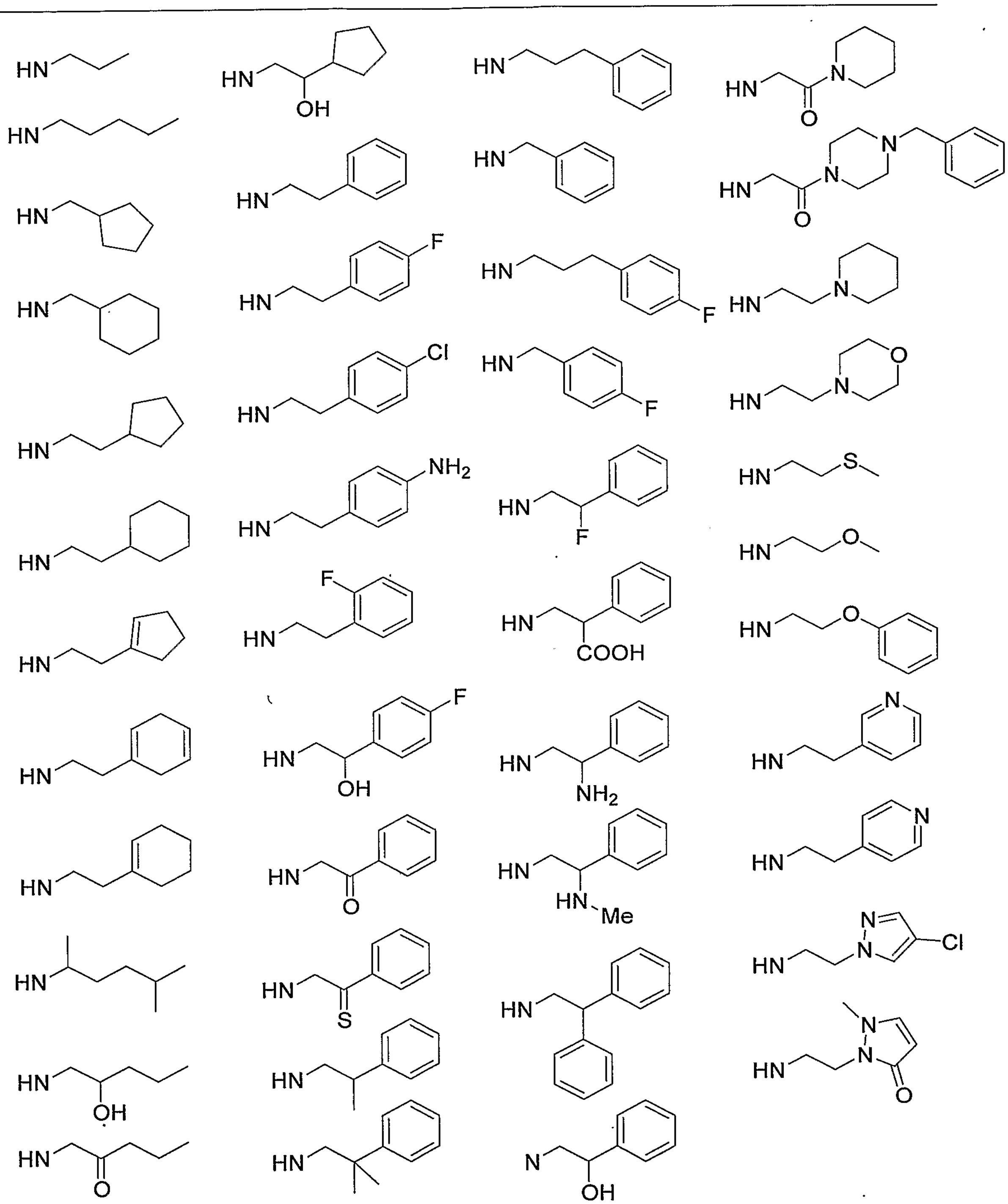

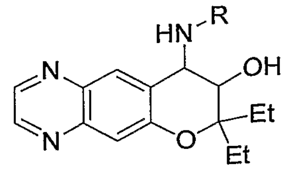

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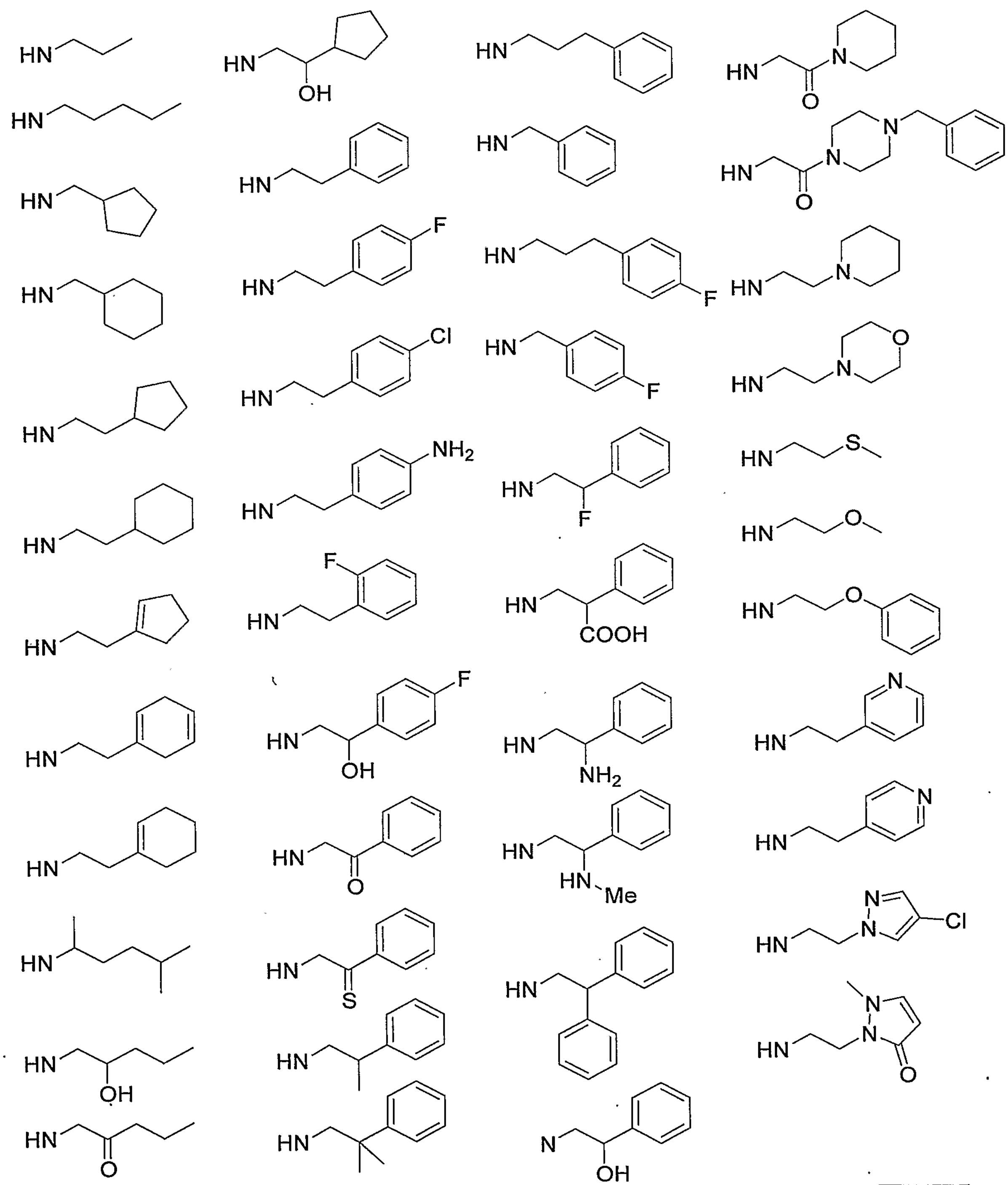

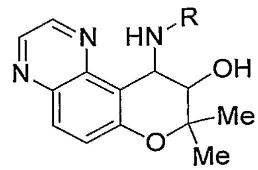

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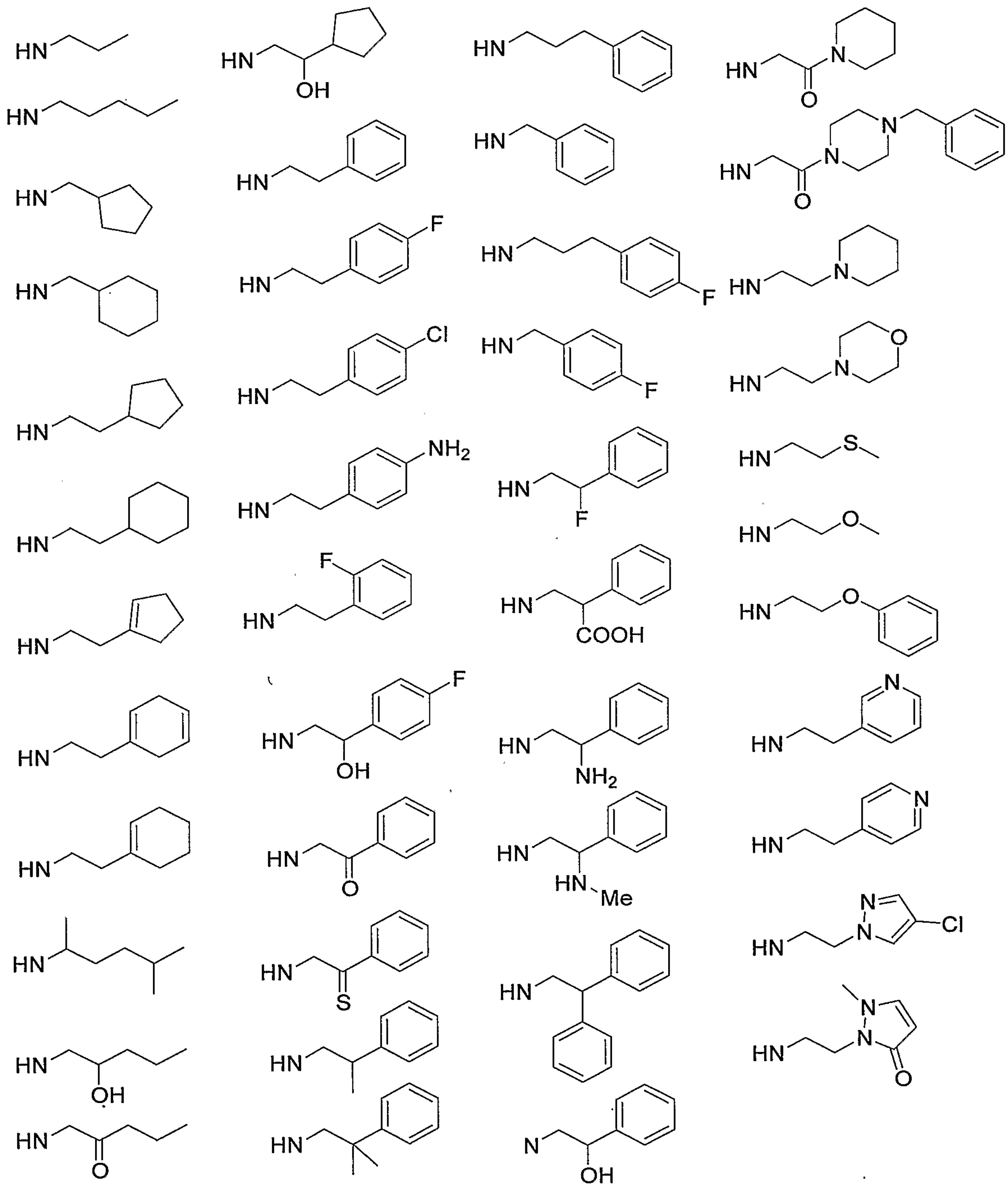

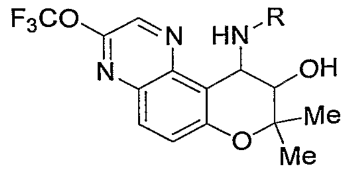

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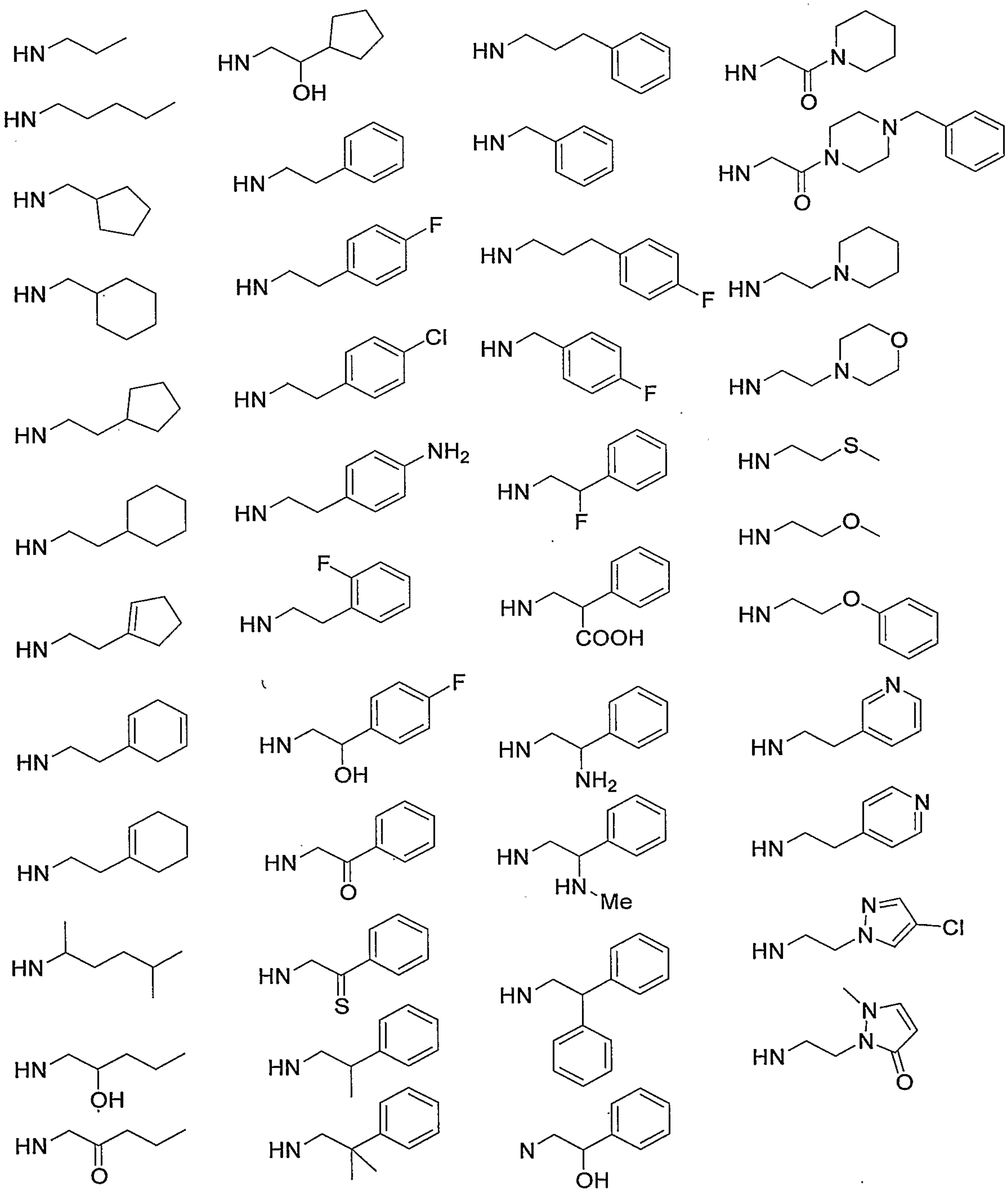

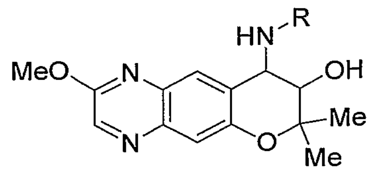

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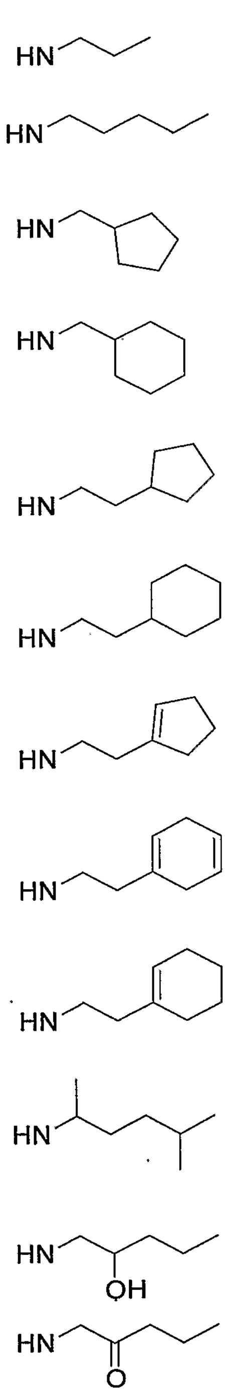
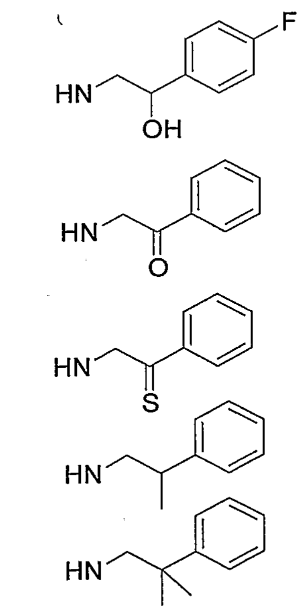
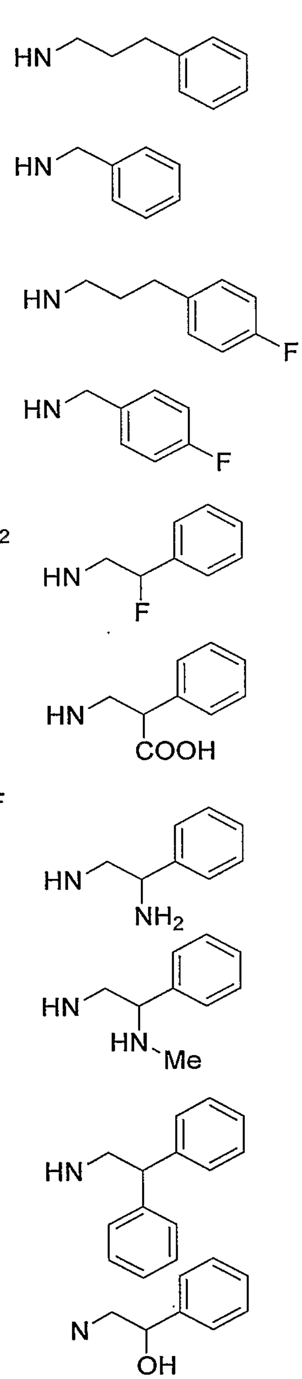
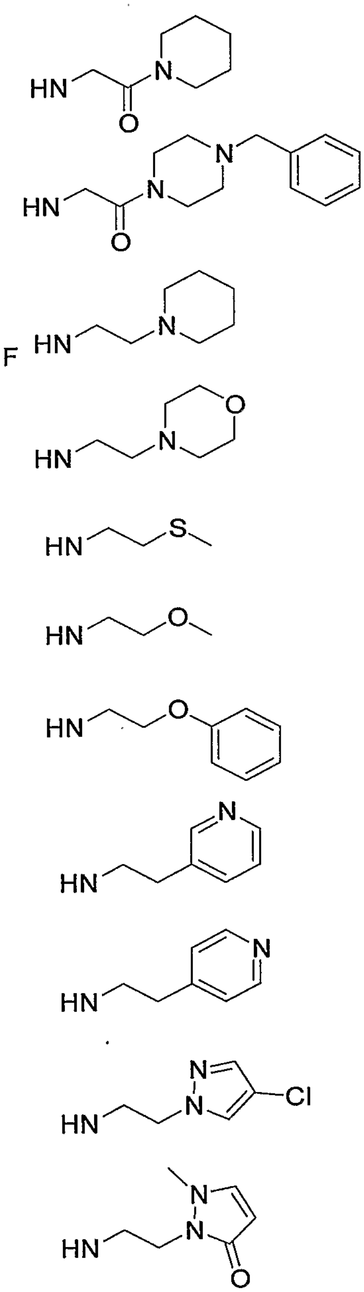

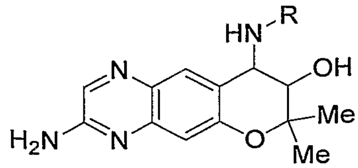

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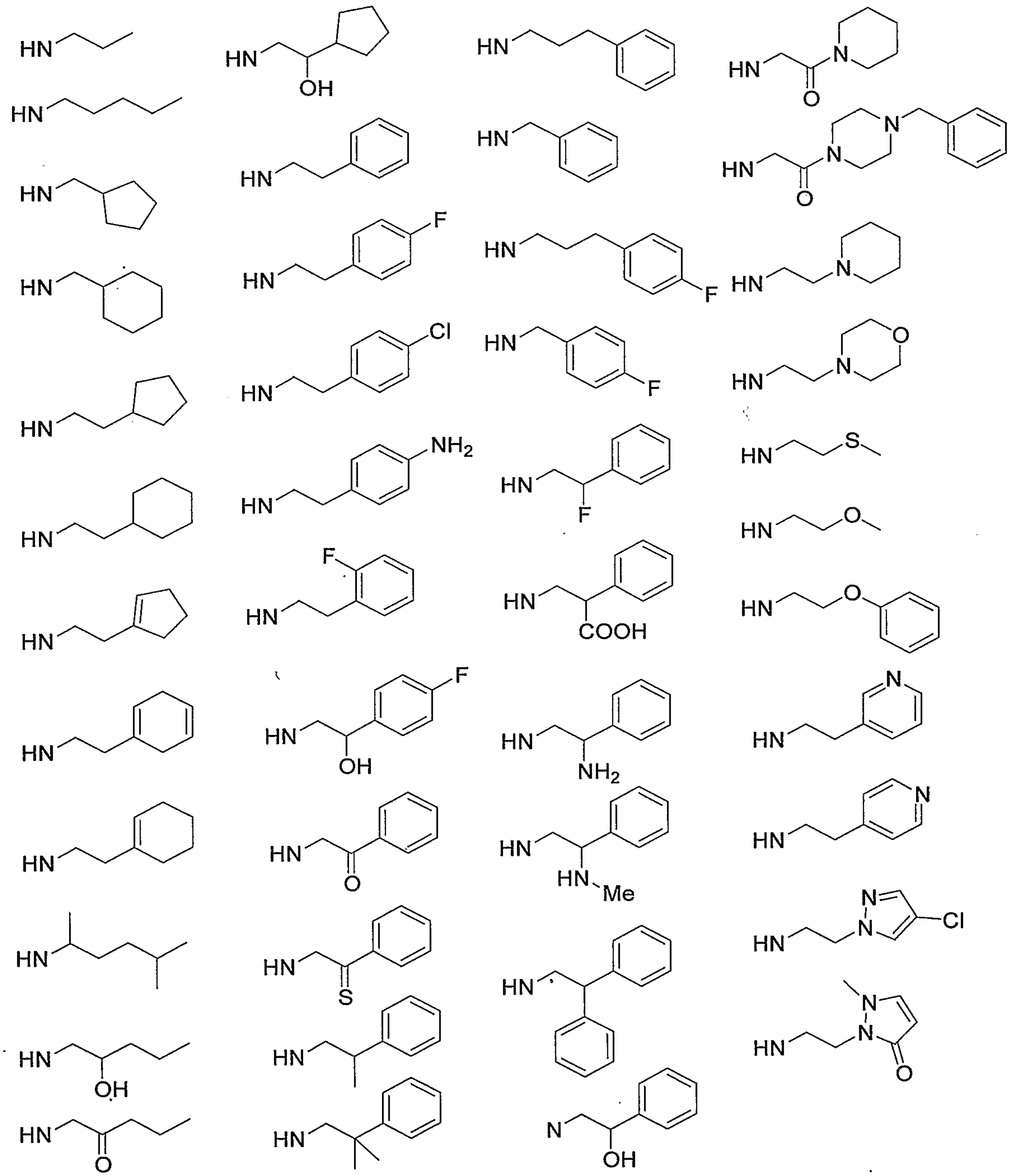

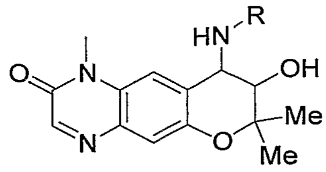

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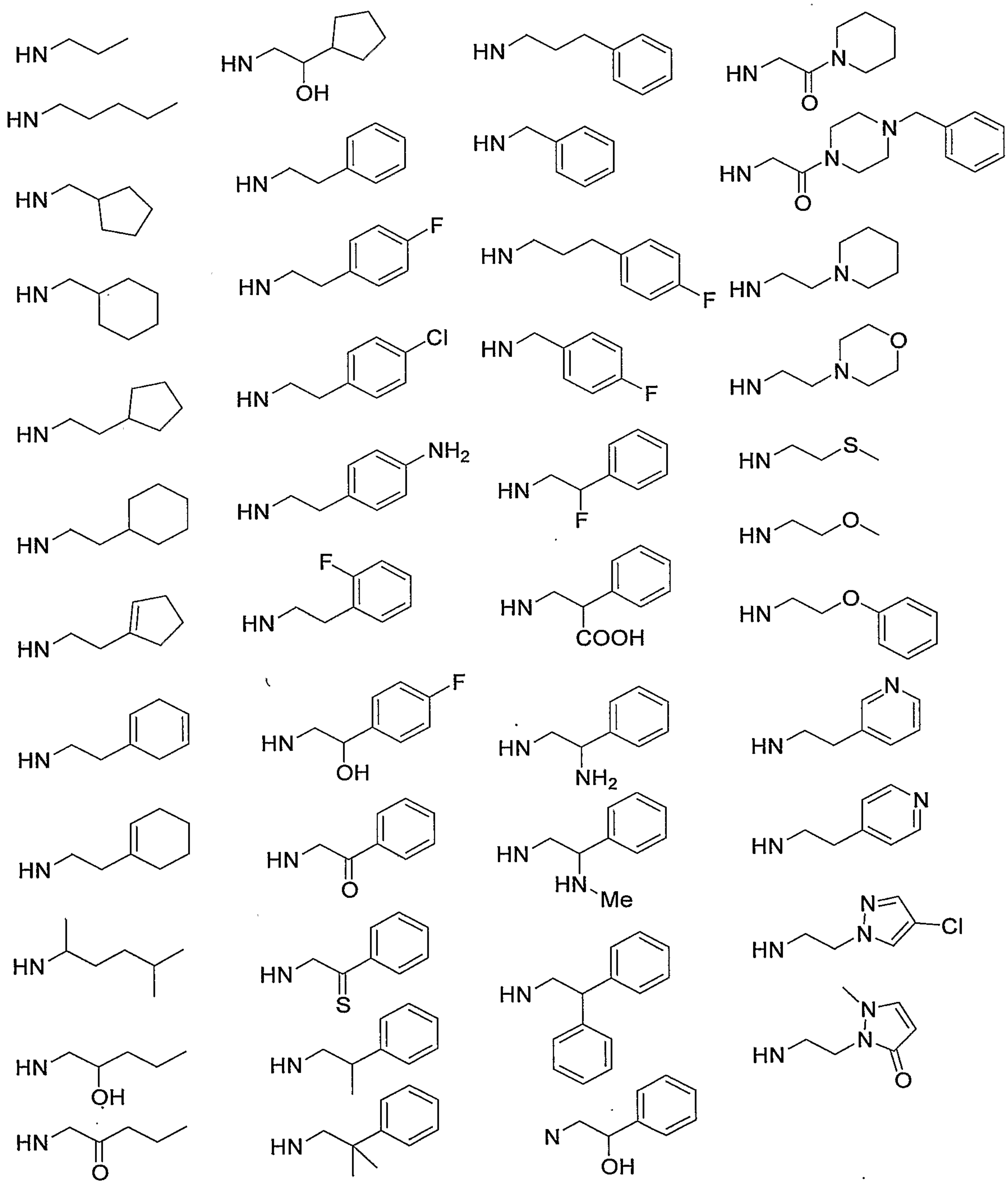

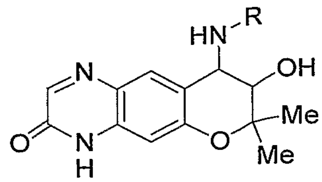

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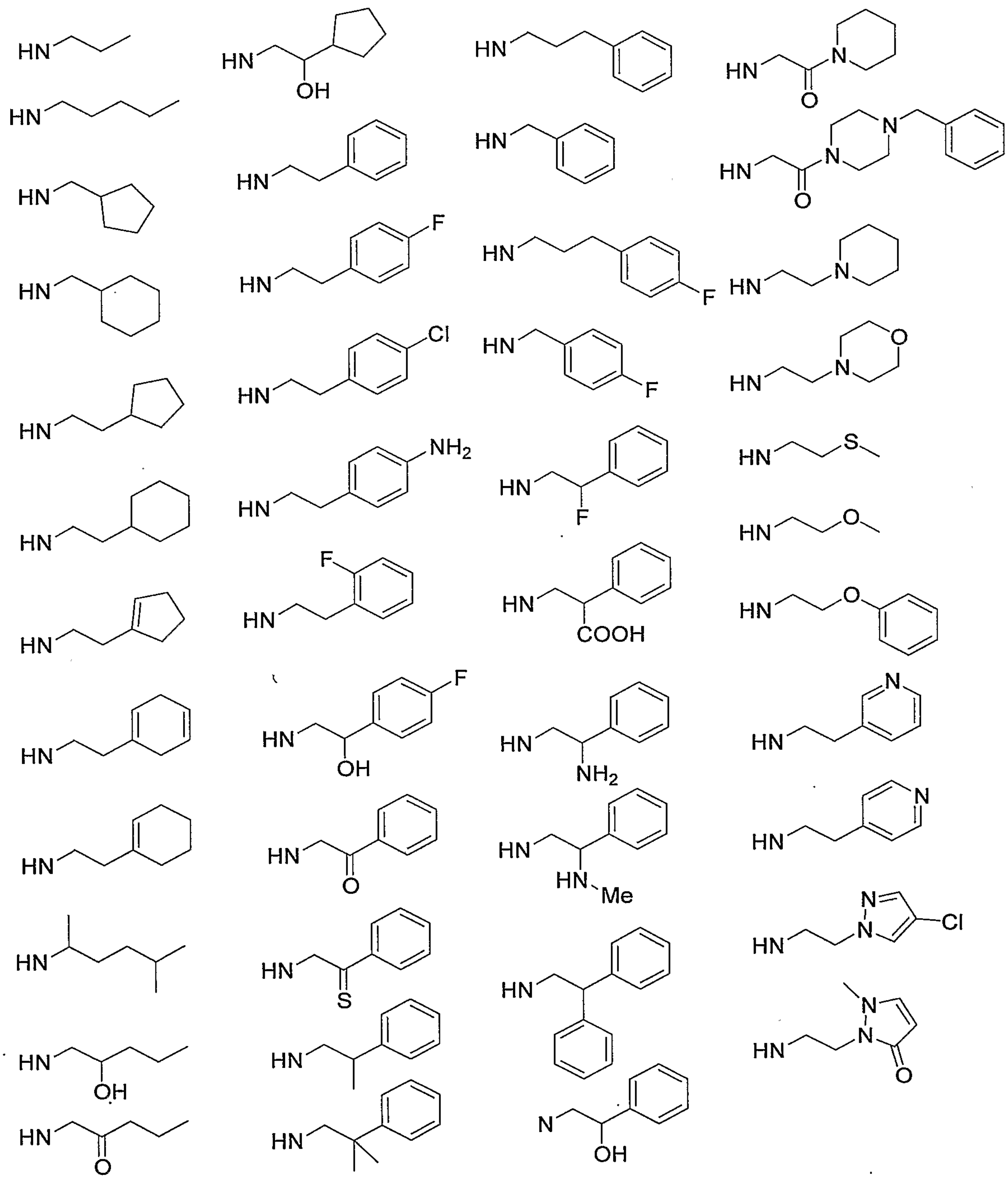

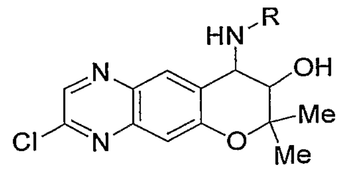

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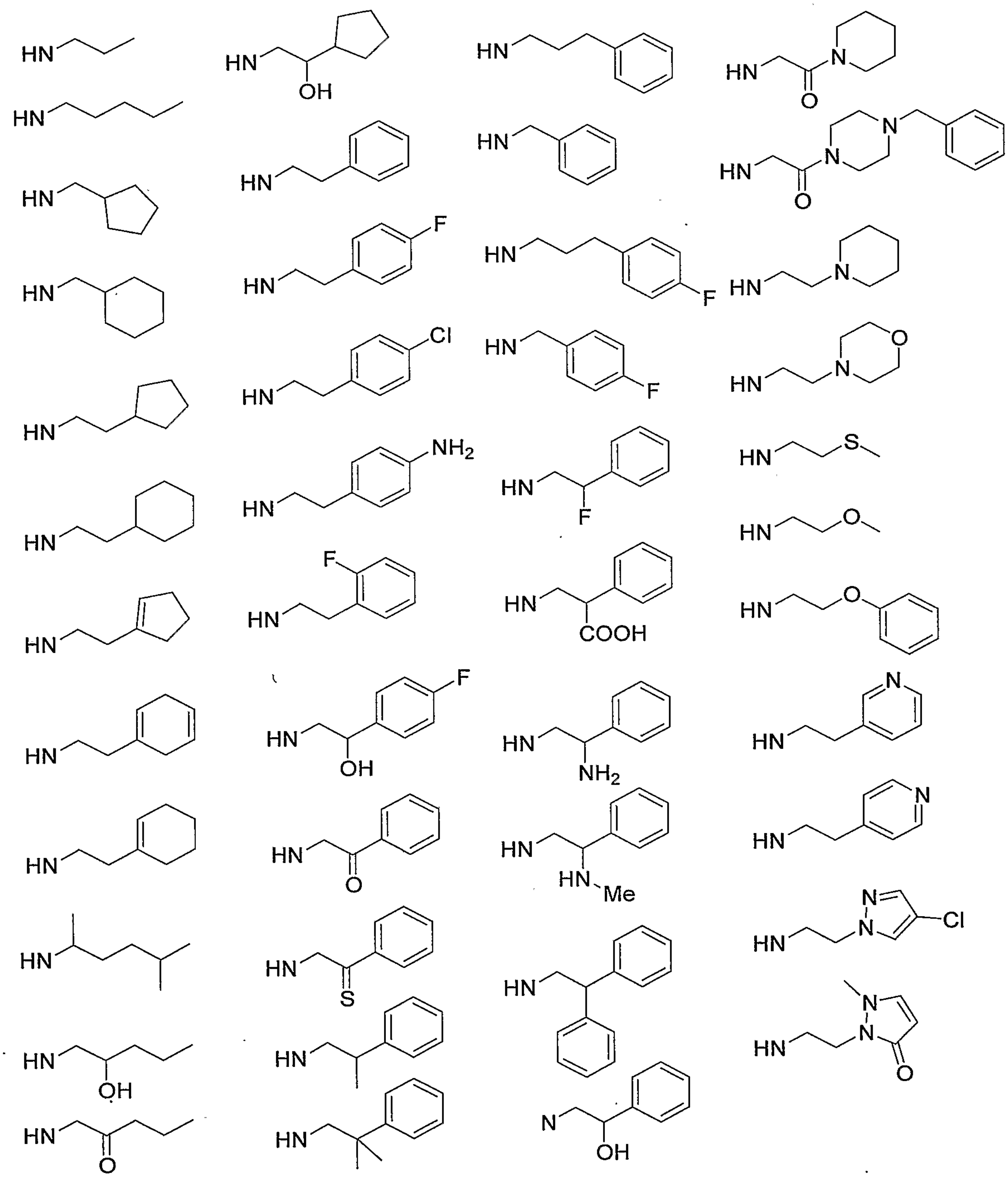

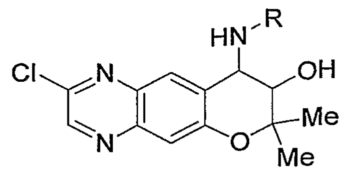

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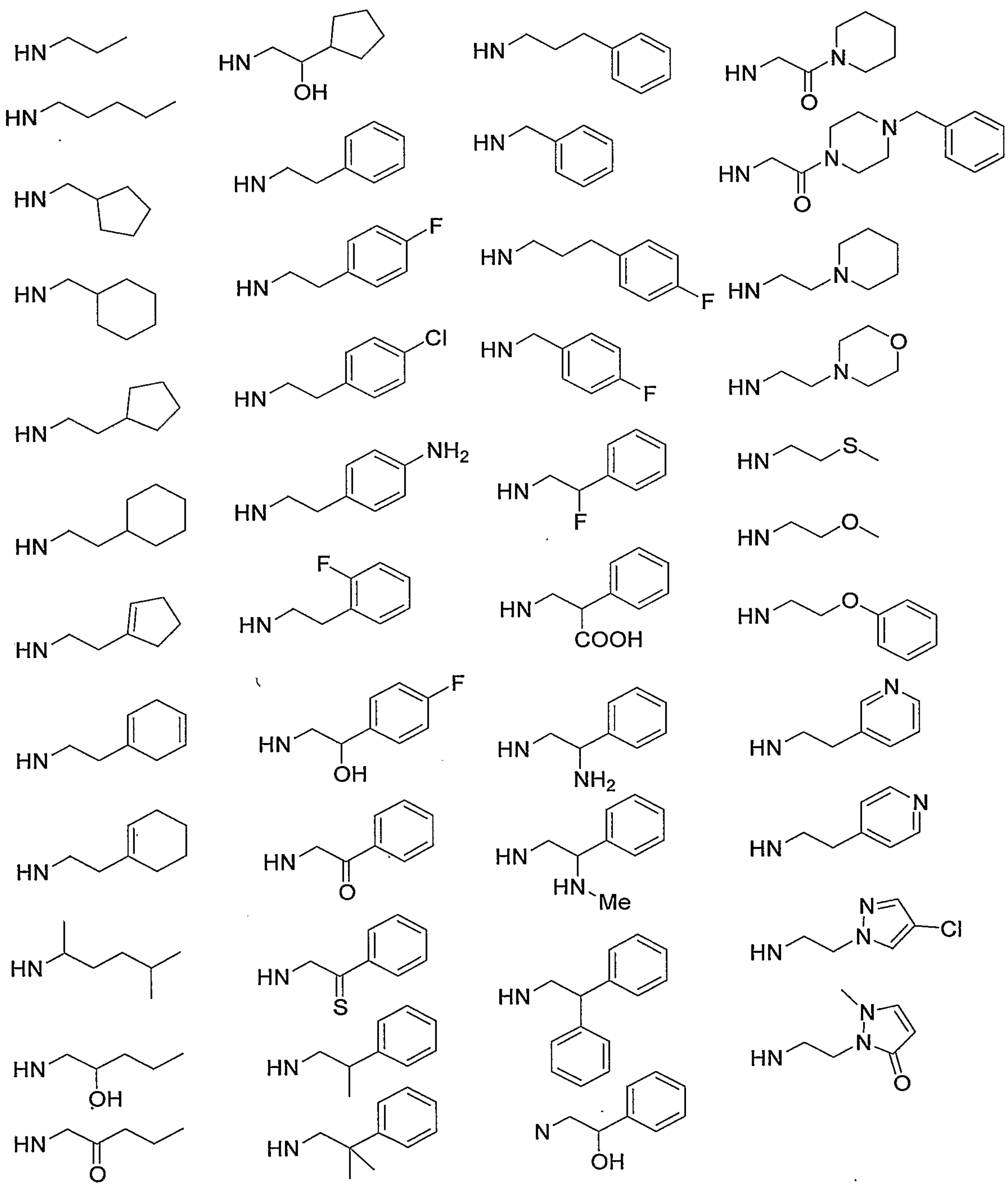

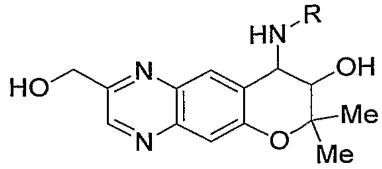

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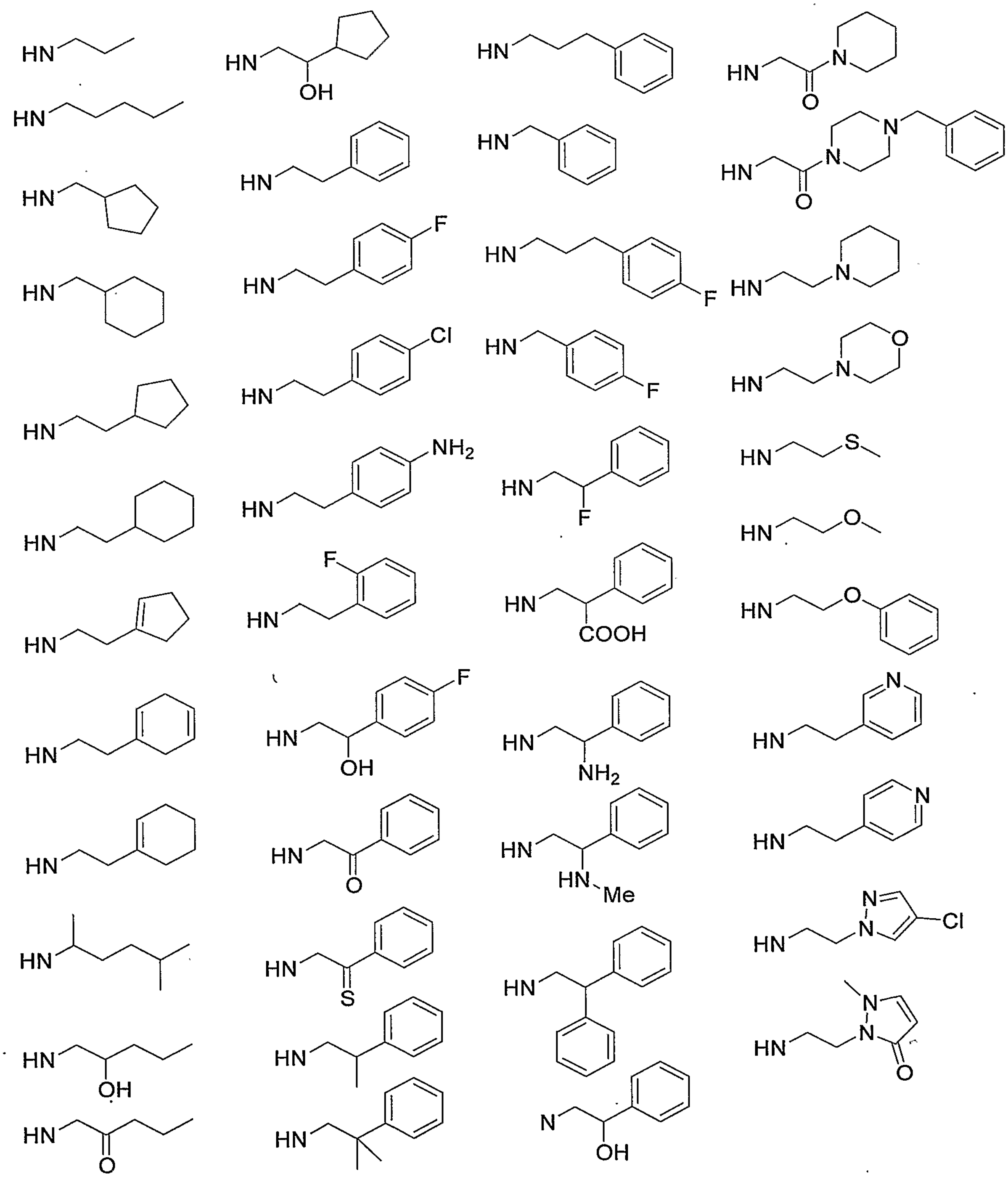

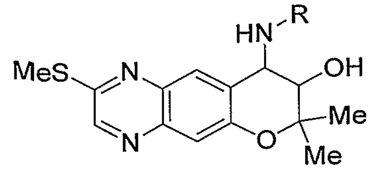

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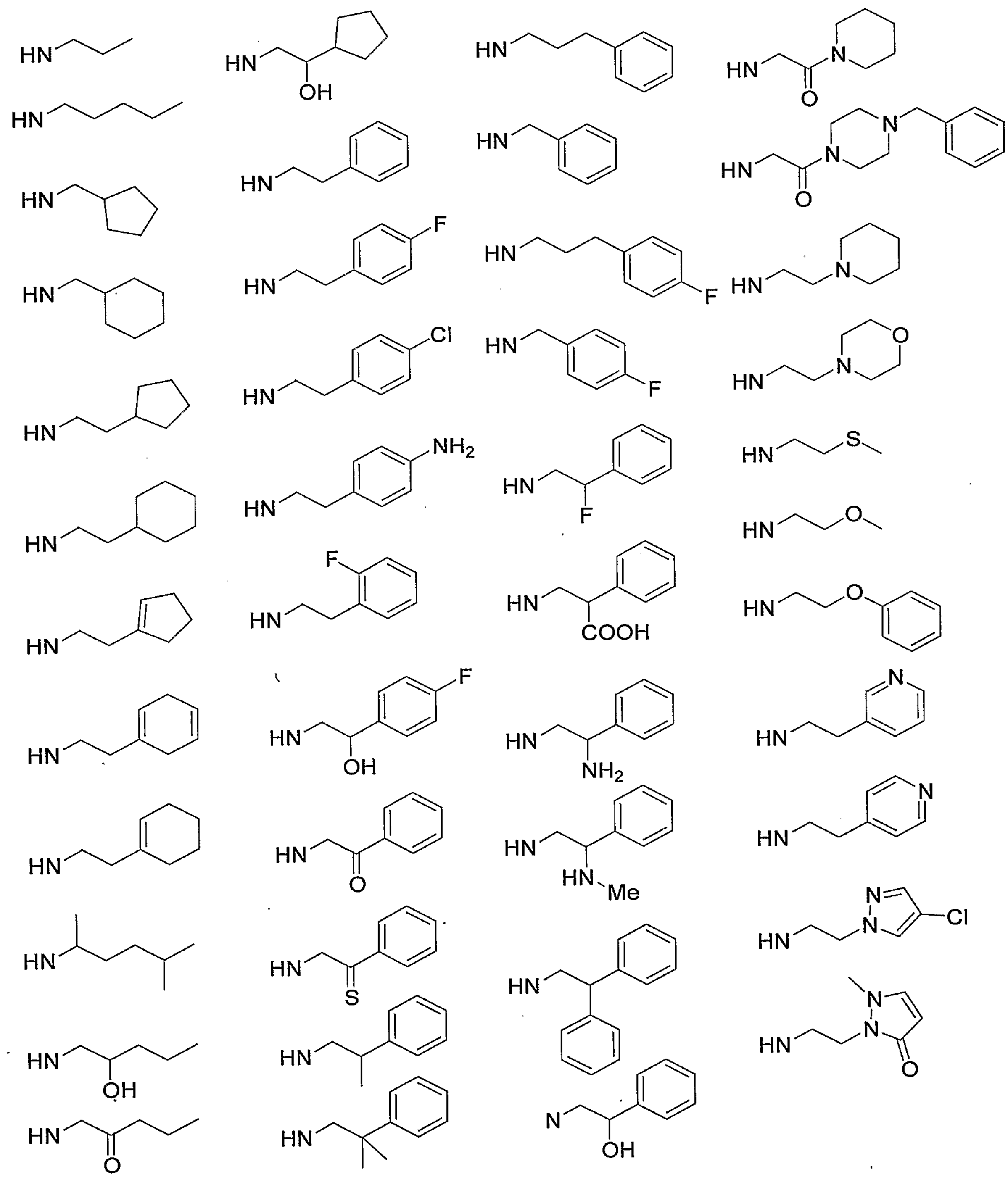

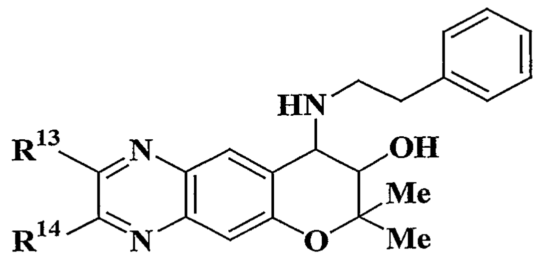

R^{13}	R^{14}	R^{13}	R^{14}	R^{13}	R^{14}
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Me	iPr	H	OMe	H	CH_2NH2
Me	nPr	Me	OEt	H	CH_2NHMe
Me	nBu	Et	OCF_3	H	CH_2Ph
Me	tBu	iPr	OnPr	Me	CH_2CH_2Ph
Et	Me	Ph	OiPr	Me	COMe
iPr	Et	H	Ph	Me	COOH
nPr	iPr	Me	SEt	Me	$CONH_2$
nBu	nPr	Et	SiPr	Me	CONHMe
tBu	nBu	iPr	NH_2	Et	CONHMs
OMe	H	H	NHMe	Et	NHMs
OEt	Me	H	NHEt	Et	NHCOMe
OiPr	Et	H	NHPh	Et	NO_2
OPh	iPr	CH_2OH	Me	iPr	CHO
SEt	H	CH_2NH2	Et	iPr	SO_3H
SiPr	Me	CH_2NHMe	iPr	iPr	SO_2NHMe
NH_2	H	CH_2Ph	H	iPr	OH
NHMe	Me	CH_2CH_2Ph	H	NHMs	Cl
NHEt	Ph	COMe	H	NHCOMe	Cl
NHPh	H	COOH	H	NO_2	Cl
Cl	Me	$CONH_2$	H	CHO	Br
Cl	Et	CONHMe	H	SO_3H	Br
Cl	Ph	CONHMs	Me	SO_2NHMe	Br
Me	Cl	NHMs	Me	OH	Br
Et	Cl	NHCOMe	Me	Cl	NHMs
Ph	Cl	NO_2	Me	Cl	NHCOMe
Br	Me	CHO	Et	Cl	NO_2
Br	Cl	SO_3H	Et	Br	CHO
Me	Br	SO_2NHMe	Et	Br	SO_3H
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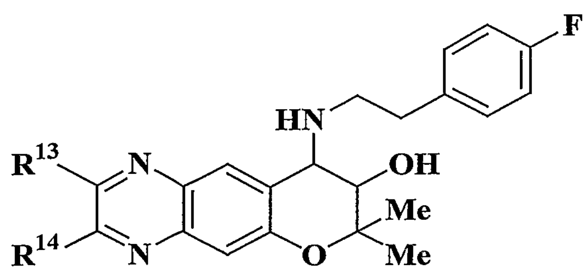

R^{13}	R^{14}	R^{13}	R^{14}	R^{13}	R^{14}
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Me	iPr	H	OMe	H	CH_2NH2
Me	nPr	Me	OEt	H	CH_2NHMe
Me	nBu	Et	OCF_3	H	CH_2Ph
Me	tBu	iPr	OnPr	Me	CH_2CH_2Ph
Et	Me	Ph	OiPr	Me	COMe
iPr	Et	H	Ph	Me	COOH
nPr	iPr	Me	SEt	Me	$CONH_2$
nBu	nPr	Et	SiPr	Me	CONHMe
tBu	nBu	iPr	NH_2	Et	CONHMs
OMe	H	H	NHMe	Et	NHMs
OEt	Me	H	NHEt	Et	NHCOMe
OiPr	Et	H	NHPh	Et	NO_2
OPh	iPr	CH_2OH	Me	iPr	CHO
SEt	H	CH_2NH2	Et	iPr	SO_3H
SiPr	Me	CH_2NHMe	iPr	iPr	SO_2NHMe
NH_2	H	CH_2Ph	H	iPr	OH
NHMe	Me	CH_2CH_2Ph	H	NHMs	Cl
NHEt	Ph	COMe	H	NHCOMe	Cl
NHPh	H	COOH	H	NO_2	Cl
Cl	Me	$CONH_2$	H	CHO	Br
Cl	Et	CONHMe	H	SO_3H	Br
Cl	Ph	CONHMs	Me	SO_2NHMe	Br
Me	Cl	NHMs	Me	OH	Br
Et	Cl	NHCOMe	Me	Cl	NHMs
Ph	Cl	NO_2	Me	Cl	NHCOMe
Br	Me	CHO	Et	Cl	NO_2
Br	Cl	SO_3H	Et	Br	CHO
Me	Br	SO_2NHMe	Et	Br	SO_3H
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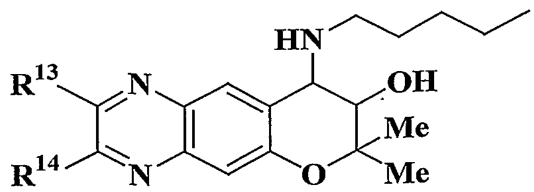
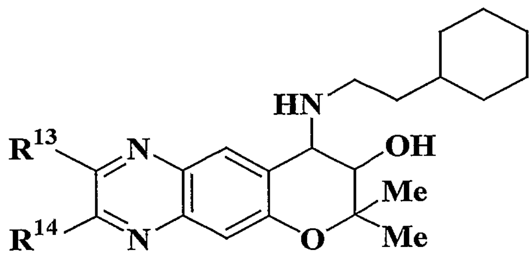
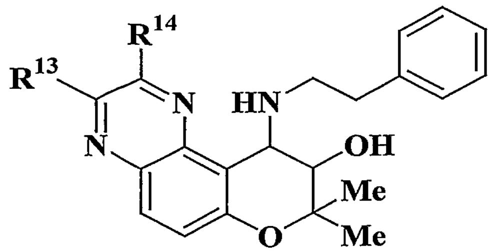


R^{13}	R^{14}	R^{13}	R^{14}	R^{13}	R^{14}
Me	Et	H	OH	H	CH_2OH
Me	iPr	H	OMe	H	CH_2NH2
Me	nPr	Me	OEt	H	CH_2NHMe
Me	nBu	Et	OCF_3	H	CH_2Ph
Me	tBu	iPr	OnPr	Me	CH_2CH_2Ph
Et	Me	Ph	OiPr	Me	COMe
iPr	Et	H	Ph	Me	COOH
nPr	iPr	Me	SEt	Me	$CONH_2$
nBu	nPr	Et	SiPr	Me	CONHMe
tBu	nBu	iPr	NH_2	Et	CONHMs
OMe	H	H	NHMe	Et	NHMs
OEt	Me	H	NHEt	Et	NHCOMe
OiPr	Et	H	NHPh	Et	NO_2
OPh	iPr	CH_2OH	Me	iPr	CHO
SEt	H	CH_2NH2	Et	iPr	SO_3H
SiPr	Me	CH_2NHMe	iPr	iPr	SO_2NHMe
NH_2	H	CH_2Ph	H	iPr	OH
NHMe	Me	CH_2CH_2Ph	H	NHMs	Cl
NHEt	Ph	COMe	H	NHCOMe	Cl
NHPh	H	COOH	H	NO_2	Cl
Cl	Me	$CONH_2$	H	CHO	Br
Cl	Et	CONHMe	H	SO_3H	Br
Cl	Ph	CONHMs	Me	SO_2NHMe	Br
Me	Cl	NHMs	Me	OH	Br
Et	Cl	NHCOMe	Me	Cl	NHMs
Ph	Cl	NO_2	Me	Cl	NHCOMe
Br	Me	CHO	Et	Cl	NO_2
Br	Cl	SO_3H	Et	Br	CHO
Me	Br	SO_2NHMe	Et	Br	SO_3H
Cl	Br	OH	Et	Br	SO_2NHMe



R^{13}	R^{14}	R^{13}	R^{14}	R^{13}	R^{14}
Me	Et	H	OH	H	CH_2OH
Me	iPr	H	OMe	H	CH_2NH2
Me	nPr	Me	OEt	H	CH_2NHMe
Me	nBu	Et	OCF_3	H	CH_2Ph
Me	tBu	iPr	OnPr	Me	CH_2CH_2Ph
Et	Me	Ph	OiPr	Me	COMe
iPr	Et	H	Ph	Me	COOH
nPr	iPr	Me	SEt	Me	$CONH_2$
nBu	nPr	Et	SiPr	Me	CONHMe
tBu	nBu	iPr	NH_2	Et	CONHMs
OMe	H	H	NHMe	Et	NHMs
OEt	Me	H	NHEt	Et	NHCOMe
OiPr	Et	H	NHPh	Et	NO_2
OPh	iPr	CH_2OH	Me	iPr	CHO
SEt	H	CH_2NH2	Et	iPr	SO_3H
SiPr	Me	CH_2NHMe	iPr	iPr	SO_2NHMe
NH_2	H	CH_2Ph	H	iPr	OH
NHMe	Me	CH_2CH_2Ph	H	NHMs	Cl
NHEt	Ph	COMe	H	NHCOMe	Cl
NHPh	H	COOH	H	NO_2	Cl
Cl	Me	$CONH_2$	H	CHO	Br
Cl	Et	CONHMe	H	SO_3H	Br
Cl	Ph	CONHMs	Me	SO_2NHMe	Br
Me	Cl	NHMs	Me	OH	Br
Et	Cl	NHCOMe	Me	Cl	NHMs
Ph	Cl	NO_2	Me	Cl	NHCOMe
Br	Me	CHO	Et	Cl	NO_2
Br	Cl	SO_3H	Et	Br	CHO
Me	Br	SO_2NHMe	Et	Br	SO_3H
Cl	Br	OH	Et	Br	SO_2NHMe



R^{13}	R^{14}
Me	Et
Me	iPr
Me	nPr
Me	nBu
Me	tBu
Et	Me
iPr	Et
nPr	iPr
nBu	nPr
tBu	nBu
OMe	H
OEt	Me
OiPr	Et
OPh	iPr
SEt	H
SiPr	Me
NH_2	H
NHMe	Me
NHEt	Ph
NHPh	H
Cl	Me
Cl	Et
Cl	Ph
Me	Cl
Et	Cl
Ph	Cl
Br	Me
Br	Cl
Me	Br
Cl	Br

R^{13}	R^{14}
H	OH
H	OMe
Me	OEt
Et	OCF_3
iPr	OnPr
Ph	OiPr
H	Ph
Me	SEt
Et	SiPr
iPr	NH_2
H	NHMe
H	NHEt
H	NHPh
CH_2OH	Me
CH_2NH2	Et
CH_2NHMe	iPr
CH_2Ph	H
CH_2CH_2Ph	H
COMe	H
COOH	H
$CONH_2$	H
CONHMe	H
CONHMs	Me
NHMs	Me
NHCOMe	Me
NO_2	Me
CHO	Et
SO_3H	Et
SO_2NHMe	Et
OH	Et

R^{13}	R^{14}
H	CH_2OH
H	CH_2NH2
H	CH_2NHMe
H	CH_2Ph
Me	CH_2CH_2Ph
Me	COMe
Me	COOH
Me	$CONH_2$
Me	CONHMe
Et	CONHMs
Et	NHMs
Et	NHCOMe
Et	NO_2
iPr	CHO
iPr	SO_3H
iPr	SO_2NHMe
iPr	OH
NHMs	Cl
NHCOMe	Cl
NO_2	Cl
CHO	Br
SO_3H	Br
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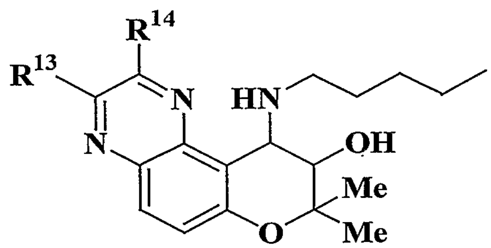
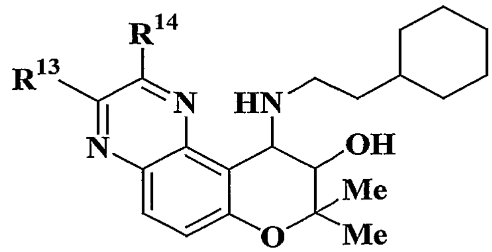
Br	SO_3H
Br	SO_2NHMe



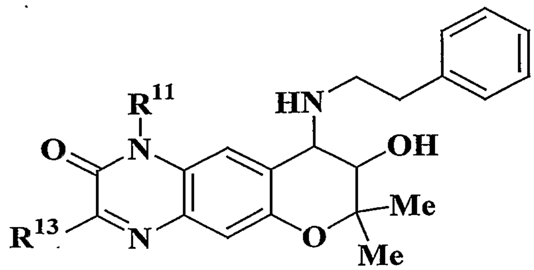
R^{13}	R^{14}	R^{13}	R^{14}	R^{13}	R^{14}
Me	Et	H	OH	H	CH_2OH
Me	iPr	H	OMe	H	CH_2NH2
Me	nPr	Me	OEt	H	CH_2NHMe
Me	nBu	Et	OCF_3	H	CH_2Ph
Me	tBu	iPr	OnPr	Me	CH_2CH_2Ph
Et	Me	Ph	OiPr	Me	COMe
iPr	Et	H	Ph	Me	COOH
nPr	iPr	Me	SEt	Me	$CONH_2$
nBu	nPr	Et	SiPr	Me	CONHMe
tBu	nBu	iPr	NH_2	Et	CONHMs
OMe	H	H	NHMe	Et	NHMs
OEt	Me	H	NHEt	Et	NHCOMe
OiPr	Et	H	NHPh	Et	NO_2
OPh	iPr	CH_2OH	Me	iPr	CHO
SEt	H	CH_2NH2	Et	iPr	SO_3H
SiPr	Me	CH_2NHMe	iPr	iPr	SO_2NHMe
NH_2	H	CH_2Ph	H	iPr	OH
NHMe	Me	CH_2CH_2Ph	H	NHMs	Cl
NHEt	Ph	COMe	H	NHCOMe	Cl
NHPh	H	COOH	H	NO_2	Cl
Cl	Me	$CONH_2$	H	CHO	Br
Cl	Et	CONHMe	H	SO_3H	Br
Cl	Ph	CONHMs	Me	SO_2NHMe	Br
Me	Cl	NHMs	Me	OH	Br
Et	Cl	NHCOMe	Me	Cl	NHMs
Ph	Cl	NO_2	Me	Cl	NHCOMe
Br	Me	CHO	Et	Cl	NO_2
Br	Cl	SO_3H	Et	Br	CHO
Me	Br	SO_2NHMe	Et	Br	SO_3H
Cl	Br	OH	Et	Br	SO_2NHMe



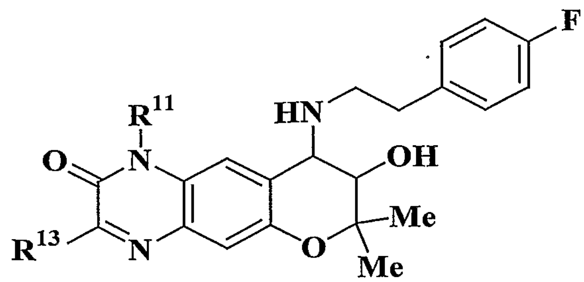
R^{13}	R^{14}
Me	Et
Me	iPr
Me	nPr
Me	nBu
Me	tBu
Et	Me
iPr	Et
nPr	iPr
nBu	nPr
tBu	nBu
OMe	H
OEt	Me
OiPr	Et
OPh	iPr
SEt	H
SiPr	Me
NH_2	H
NHMe	Me
NHEt	Ph
NHPh	H
Cl	Me
Cl	Et
Cl	Ph
Me	Cl
Et	Cl
Ph	Cl
Br	Me
Br	Cl
Me	Br
Cl	Br

R^{13}	R^{14}
H	OH
H	OMe
Me	OEt
Et	OCF_3
iPr	OnPr
Ph	OiPr
H	Ph
Me	SEt
Et	SiPr
iPr	NH_2
H	NHMe
H	NHEt
H	NHPh
CH_2OH	Me
CH_2NH2	Et
CH_2NHMe	iPr
CH_2Ph	H
CH_2CH_2Ph	H
COMe	H
COOH	H
$CONH_2$	H
CONHMe	H
CONHMs	Me
NHMs	Me
NHCOMe	Me
NO_2	Me
CHO	Et
SO_3H	Et
SO_2NHMe	Et
OH	Et

R^{13}	R^{14}
H	CH_2OH
H	CH_2NH2
H	CH_2NHMe
H	CH_2Ph
Me	CH_2CH_2Ph
Me	COMe
Me	COOH
Me	$CONH_2$
Me	CONHMe
Et	CONHMs
Et	NHMs
Et	NHCOMe
Et	NO_2
iPr	CHO
iPr	SO_3H
iPr	SO_2NHMe
iPr	OH
NHMs	Cl
NHCOMe	Cl
NO_2	Cl
CHO	Br
SO_3H	Br
SO_2NHMe	Br
OH	Br
Cl	NHMs
Cl	NHCOMe
Cl	NO_2
Br	CHO
Br	SO_3H
Br	SO_2NHMe



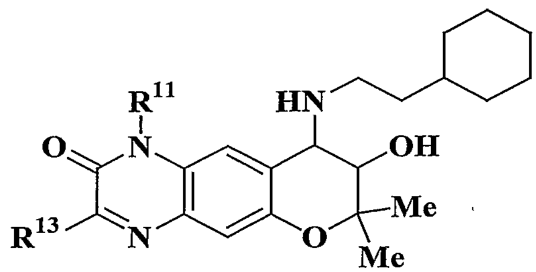
R^{11}	R^{13}	R^{11}	R^{13}	R^{11}	R^{13}
H	Et	H	Cl	H	OMe
H	iPr	H	Br	H	OCF_3
H	nPr	H	NO_2	H	OEt
H	nBu	H	CHO	H	OiPr
H	tBu	H	SO_3H	H	SMe
Me	H	Me	Cl	Me	OMe
Me	Me	Me	Br	Me	OCF_3
Me	Et	Me	CH_2OH	Me	OEt
Me	iPr	Me	CH_2NH_2	Me	SMe
Me	nPr	Me	CH_2NHMe	Me	OiPr
Me	nBu	Me	CH_2Ph	Me	OnPr
Et	H	Et	COMe	Et	NHMe
Et	Me	Et	COOH	Et	NHEt
Et	Et	Et	$CONH_2$	Et	NMe_2
iPr	H	iPr	CONHMe	iPr	NMeEt
nPr	Me	nPr	CONHMs	nPr	OMe
nBu	Et	nBu	NHMs	nBu	OCF_3
tBu	Me	tBu	NHCOMe	tBu	OEt
Ph	Ph	Ph	NO_2	Ph	OiPr
CH_2OH	H	CH_2OH	CHO	CH_2OH	SMe
CH_2OH	Me	CH_2OH	SO_3H	CH_2OH	OPh
CH_2OMe	Et	CH_2OMe	SO_2NHMe	CH_2OMe	SPh
CH_2OMe	Ph	CH_2OMe	OH	CH_2OMe	NHPh
CH_2NH_2	H	CH_2NH_2	COMe	CH_2NH_2	OMe
CH_2NH_2	Me	CH_2NH_2	COOH	CH_2NH_2	OCF_3
CH_2NH_2	Et	CH_2NH_2	$CONH_2$	CH_2NH_2	OEt
CH_2NHMe	Me	CH_2NHMe	CONHMe	CH_2NHMe	OiPr
CH_2Ph	Me	CH_2Ph	CONHMs	CH_2Ph	SMe
CH_2Ph	Et	CH_2Ph	NHMs	CH_2Ph	OPh
CH_2CH_2Ph	iPr	CH_2CH_2Ph	NO_2	CH_2CH_2Ph	SPh



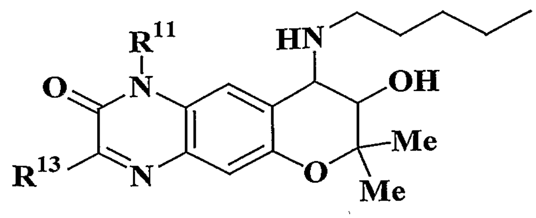
R^{11}	R^{13}
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
Me	H
Me	Me
Me	Et
Me	iPr
Me	nPr
Me	nBu
Et	H
Et	Me
Et	Et
iPr	H
nPr	Me
nBu	Et
tBu	Me
Ph	Ph
CH_2OH	H
CH_2OH	Me
CH_2OMe	Et
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	Me
CH_2NH_2	Et
CH_2NHMe	Me
CH_2Ph	Me
CH_2Ph	Et
CH_2CH_2Ph	iPr

R^{11}	R^{13}
H	Cl
H	Br
H	NO_2
H	CHO
H	SO_3H
Me	Cl
Me	Br
Me	CH_2OH
Me	CH_2NH_2
Me	CH_2NHMe
Me	CH_2Ph
Et	COMe
Et	COOH
Et	$CONH_2$
iPr	CONHMe
nPr	CONHMs
nBu	NHMs
tBu	NHCOMe
Ph	NO_2
CH_2OH	CHO
CH_2OH	SO_3H
CH_2OMe	SO_2NHMe
CH_2OMe	OH
CH_2NH_2	COMe
CH_2NH_2	COOH
CH_2NH_2	$CONH_2$
CH_2NHMe	CONHMe
CH_2Ph	CONHMs
CH_2Ph	NHMs
CH_2CH_2Ph	NO_2

R^{11}	R^{13}
H	OMe
H	OCF_3
H	OEt
H	OiPr
H	SMe
Me	OMe
Me	OCF_3
Me	OEt
Me	SMe
Me	OiPr
Me	OnPr
Et	NHMe
Et	NHEt
Et	NMe_2
iPr	NMeEt
nPr	OMe
nBu	OCF_3
tBu	OEt
Ph	OiPr
CH_2OH	SMe
CH_2OH	OPh
CH_2OMe	SPh
CH_2OMe	NHPh
CH_2NH_2	OMe
CH_2NH_2	OCF_3
CH_2NH_2	OEt
CH_2NHMe	OiPr
CH_2Ph	SMe
CH_2Ph	OPh
CH_2CH_2Ph	SPh



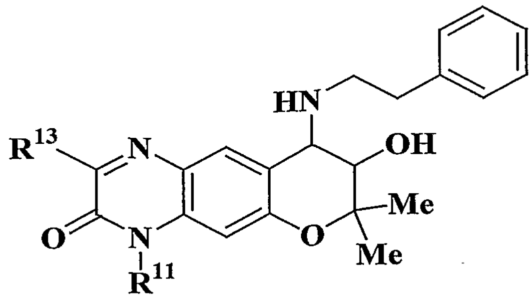
R^{11}	R^{13}	R^{11}	R^{13}	R^{11}	R^{13}
H	Et	H	Cl	H	OMe
H	iPr	H	Br	H	OCF_3
H	nPr	H	NO_2	H	OEt
H	nBu	H	CHO	H	OiPr
H	tBu	H	SO_3H	H	SMe
Me	H	Me	Cl	Me	OMe
Me	Me	Me	Br	Me	OCF_3
Me	Et	Me	CH_2OH	Me	OEt
Me	iPr	Me	CH_2NH_2	Me	SMe
Me	nPr	Me	CH_2NHMe	Me	OiPr
Me	nBu	Me	CH_2Ph	Me	OnPr
Et	H	Et	COMe	Et	NHMe
Et	Me	Et	COOH	Et	NHEt
Et	Et	Et	$CONH_2$	Et	NMe_2
iPr	H	iPr	CONHMe	iPr	NMeEt
nPr	Me	nPr	CONHMs	nPr	OMe
nBu	Et	nBu	NHMs	nBu	OCF_3
tBu	Me	tBu	NHCOMe	tBu	OEt
Ph	Ph	Ph	NO_2	Ph	OiPr
CH_2OH	H	CH_2OH	CHO	CH_2OH	SMe
CH_2OH	Me	CH_2OH	SO_3H	CH_2OH	OPh
CH_2OMe	Et	CH_2OMe	SO_2NHMe	CH_2OMe	SPh
CH_2OMe	Ph	CH_2OMe	OH	CH_2OMe	NHPh
CH_2NH_2	H	CH_2NH_2	COMe	CH_2NH_2	OMe
CH_2NH_2	Me	CH_2NH_2	COOH	CH_2NH_2	OCF_3
CH_2NH_2	Et	CH_2NH_2	$CONH_2$	CH_2NH_2	OEt
CH_2NHMe	Me	CH_2NHMe	CONHMe	CH_2NHMe	OiPr
CH_2Ph	Me	CH_2Ph	CONHMs	CH_2Ph	SMe
CH_2Ph	Et	CH_2Ph	NHMs	CH_2Ph	OPh
CH_2CH_2Ph	iPr	CH_2CH_2Ph	NO_2	CH_2CH_2Ph	SPh



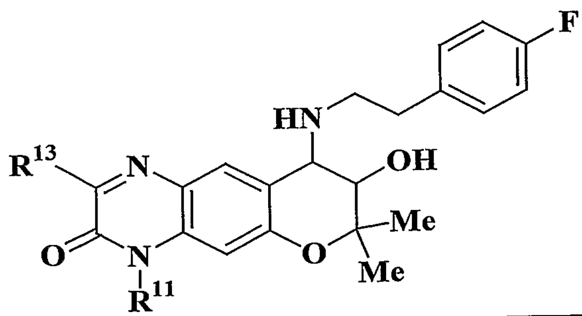
R^{11}	R^{13}
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
Me	H
Me	Me
Me	Et
Me	iPr
Me	nPr
Me	nBu
Et	H
Et	Me
Et	Et
iPr	H
nPr	Me
nBu	Et
tBu	Me
Ph	Ph
CH_2OH	H
CH_2OH	Me
CH_2OMe	Et
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	Me
CH_2NH_2	Et
CH_2NHMe	Me
CH_2Ph	Me
CH_2Ph	Et
CH_2CH_2Ph	iPr

R^{11}	R^{13}
H	Cl
H	Br
H	NO_2
H	CHO
H	SO_3H
Me	Cl
Me	Br
Me	CH_2OH
Me	CH_2NH_2
Me	CH_2NHMe
Me	CH_2Ph
Et	COMe
Et	COOH
Et	$CONH_2$
iPr	CONHMe
nPr	CONHMs
nBu	NHMs
tBu	NHCOMe
Ph	NO_2
CH_2OH	CHO
CH_2OH	SO_3H
CH_2OMe	SO_2NHMe
CH_2OMe	OH
CH_2NH_2	COMe
CH_2NH_2	COOH
CH_2NH_2	$CONH_2$
CH_2NHMe	CONHMe
CH_2Ph	CONHMs
CH_2Ph	NHMs
CH_2CH_2Ph	NO_2

R^{11}	R^{13}
H	OMe
H	OCF_3
H	OEt
H	OiPr
H	SMe
Me	OMe
Me	OCF_3
Me	OEt
Me	SMe
Me	OiPr
Me	OnPr
Et	NHMe
Et	NHEt
Et	NMe_2
iPr	NMeEt
nPr	OMe
nBu	OCF_3
tBu	OEt
Ph	OiPr
CH_2OH	SMe
CH_2OH	OPh
CH_2OMe	SPh
CH_2OMe	NHPh
CH_2NH_2	OMe
CH_2NH_2	OCF_3
CH_2NH_2	OEt
CH_2NHMe	OiPr
CH_2Ph	SMe
CH_2Ph	OPh
CH_2CH_2Ph	SPh



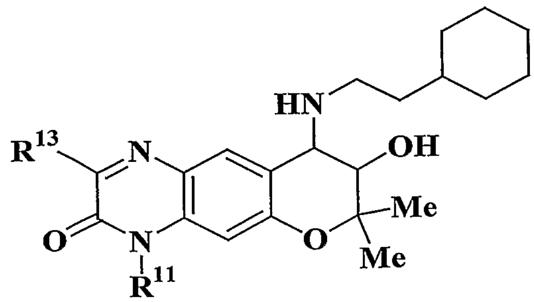
R^{11}	R^{13}	R^{11}	R^{13}	R^{11}	R^{13}
H	Et	H	Cl	H	OMe
H	iPr	H	Br	H	OCF_3
H	nPr	H	NO_2	H	OEt
H	nBu	H	CHO	H	OiPr
H	tBu	H	SO_3H	H	SMe
Me	H	Me	Cl	Me	OMe
Me	Me	Me	Br	Me	OCF_3
Me	Et	Me	CH_2OH	Me	OEt
Me	iPr	Me	CH_2NH_2	Me	SMe
Me	nPr	Me	CH_2NHMe	Me	OiPr
Me	nBu	Me	CH_2Ph	Me	OnPr
Et	H	Et	COMe	Et	NHMe
Et	Me	Et	COOH	Et	NHEt
Et	Et	Et	$CONH_2$	Et	NMe_2
iPr	H	iPr	CONHMe	iPr	NMeEt
nPr	Me	nPr	CONHMs	nPr	OMe
nBu	Et	nBu	NHMs	nBu	OCF_3
tBu	Me	tBu	NHCOMe	tBu	OEt
Ph	Ph	Ph	NO_2	Ph	OiPr
CH_2OH	H	CH_2OH	CHO	CH_2OH	SMe
CH_2OH	Me	CH_2OH	SO_3H	CH_2OH	OPh
CH_2OMe	Et	CH_2OMe	SO_2NHMe	CH_2OMe	SPh
CH_2OMe	Ph	CH_2OMe	OH	CH_2OMe	NHPh
CH_2NH_2	H	CH_2NH_2	COMe	CH_2NH_2	OMe
CH_2NH_2	Me	CH_2NH_2	COOH	CH_2NH_2	OCF_3
CH_2NH_2	Et	CH_2NH_2	$CONH_2$	CH_2NH_2	OEt
CH_2NHMe	Me	CH_2NHMe	CONHMe	CH_2NHMe	OiPr
CH_2Ph	Me	CH_2Ph	CONHMs	CH_2Ph	SMe
CH_2Ph	Et	CH_2Ph	NHMs	CH_2Ph	OPh
CH_2CH_2Ph	iPr	CH_2CH_2Ph	NO_2	CH_2CH_2Ph	SPh



R^{11}	R^{13}
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
Me	H
Me	Me
Me	Et
Me	iPr
Me	nPr
Me	nBu
Et	H
Et	Me
Et	Et
iPr	H
nPr	Me
nBu	Et
tBu	Me
Ph	Ph
CH_2OH	H
CH_2OH	Me
CH_2OMe	Et
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	Me
CH_2NH_2	Et
CH_2NHMe	Me
CH_2Ph	Me
CH_2Ph	Et
CH_2CH_2Ph	iPr

R^{11}	R^{13}
H	Cl
H	Br
H	NO_2
H	CHO
H	SO_3H
Me	Cl
Me	Br
Me	CH_2OH
Me	CH_2NH_2
Me	CH_2NHMe
Me	CH_2Ph
Et	COMe
Et	COOH
Et	$CONH_2$
iPr	CONHMe
nPr	CONHMs
nBu	NHMs
tBu	NHCOMe
Ph	NO_2
CH_2OH	CHO
CH_2OH	SO_3H
CH_2OMe	SO_2NHMe
CH_2OMe	OH
CH_2NH_2	COMe
CH_2NH_2	COOH
CH_2NH_2	$CONH_2$
CH_2NHMe	CONHMe
CH_2Ph	CONHMs
CH_2Ph	NHMs
CH_2CH_2Ph	NO_2

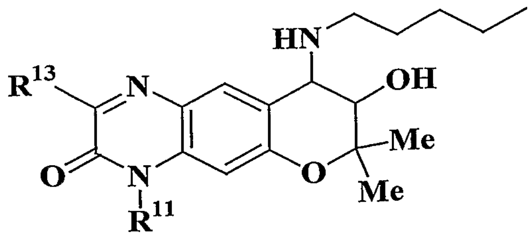
R^{11}	R^{13}
H	OMe
H	OCF_3
H	OEt
H	OiPr
H	SMe
Me	OMe
Me	OCF_3
Me	OEt
Me	SMe
Me	OiPr
Me	OnPr
Et	NHMe
Et	NHEt
Et	NMe_2
iPr	NMeEt
nPr	OMe
nBu	OCF_3
tBu	OEt
Ph	OiPr
CH_2OH	SMe
CH_2OH	OPh
CH_2OMe	SPh
CH_2OMe	NHPh
CH_2NH_2	OMe
CH_2NH_2	OCF_3
CH_2NH_2	OEt
CH_2NHMe	OiPr
CH_2Ph	SMe
CH_2Ph	OPh
CH_2CH_2Ph	SPh



R^{11}	R^{13}
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
Me	H
Me	Me
Me	Et
Me	iPr
Me	nPr
Me	nBu
Et	H
Et	Me
Et	Et
iPr	H
nPr	Me
nBu	Et
tBu	Me
Ph	Ph
CH_2OH	H
CH_2OH	Me
CH_2OMe	Et
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	Me
CH_2NH_2	Et
CH_2NHMe	Me
CH_2Ph.	Me
CH_2Ph	Et
CH_2CH_2Ph	iPr

R^{11}	R^{13}
H	Cl
H	Br
H	NO_2
H	CHO
H	SO_3H
Me	Cl
Me	Br
Me	CH_2OH
Me	CH_2NH_2
Me	CH_2NHMe
Me	CH_2Ph
Et	COMe
Et	COOH
Et	$CONH_2$
iPr	CONHMe
nPr	CONHMs
nBu	NHMs
tBu	NHCOMe
Ph	NO_2
CH_2OH	CHO
CH_2OH	SO_3H
CH_2OMe	SO_2NHMe
CH_2OMe	OH
CH_2NH_2	COMe
CH_2NH_2	COOH
CH_2NH_2	$CONH_2$
CH_2NHMe	CONHMe
CH_2Ph	CONHMs
CH_2Ph	NHMs
CH_2CH_2Ph	NO_2

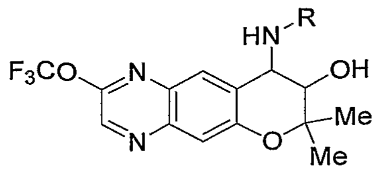
R^{11}	R^{13}
H	OMe
H	OCF_3
H	OEt
H	OiPr
H	SMe
Me	OMe
Me	OCF_3
Me	OEt
Me	SMe
Me	OiPr
Me	OnPr
Et	NHMe
Et	NHEt
Et	NMe_2
iPr	NMeEt
nPr	OMe
nBu	OCF_3
tBu	OEt
Ph	OiPr
CH_2OH	SMe
CH_2OH	OPh
CH_2OMe	SPh
CH_2OMe	NHPh
CH_2NH_2	OMe
CH_2NH_2	OCF_3
CH_2NH_2	OEt
CH_2NHMe	OiPr
CH_2Ph	SMe
CH_2Ph	OPh
CH_2CH_2Ph	SPh



R^{11}	R^{13}
H	Et
H	iPr
H	nPr
H	nBu
H	tBu
Me	H
Me	Me
Me	Et
Me	iPr
Me	nPr
Me	nBu
Et	H
Et	Me
Et	Et
iPr	H
nPr	Me
nBu	Et
tBu	Me
Ph	Ph
CH_2OH	H
CH_2OH	Me
CH_2OMe	Et
CH_2OMe	Ph
CH_2NH_2	H
CH_2NH_2	Me
CH_2NH_2	Et
CH_2NHMe	Me
CH_2Ph	Me
CH_2Ph	Et
CH_2CH_2Ph	iPr

R^{11}	R^{13}
H	Cl
H	Br
H	NO_2
H	CHO
H	SO_3H
Me	Cl
Me	Br
Me	CH_2OH
Me	CH_2NH_2
Me	CH_2NHMe
Me	CH_2Ph
Et	COMe
Et	COOH
Et	$CONH_2$
iPr	CONHMe
nPr	CONHMs
nBu	NHMs
tBu	NHCOMe
Ph	NO_2
CH_2OH	CHO
CH_2OH	SO_3H
CH_2OMe	SO_2NHMe
CH_2OMe	OH
CH_2NH_2	COMe
CH_2NH_2	COOH
CH_2NH_2	$CONH_2$
CH_2NHMe	CONHMe
CH_2Ph	CONHMs
CH_2Ph	NHMs
CH_2CH_2Ph	NO_2

R^{11}	R^{13}
H	OMe
H	OCF_3
H	OEt
H	OiPr
H	SMe
Me	OMe
Me	OCF_3
Me	OEt
Me	SMe
Me	OiPr
Me	OnPr
Et	NHMe
Et	NHEt
Et	NMe_2
iPr	NMeEt
nPr	OMe
nBu	OCF_3
tBu	OEt
Ph	OiPr
CH_2OH	SMe
CH_2OH	OPh
CH_2OMe	SPh
CH_2OMe	NHPh
CH_2NH_2	OMe
CH_2NH_2	OCF_3
CH_2NH_2	OEt
CH_2NHMe	OiPr
CH_2Ph	SMe
CH_2Ph	OPh
CH_2CH_2Ph	SPh



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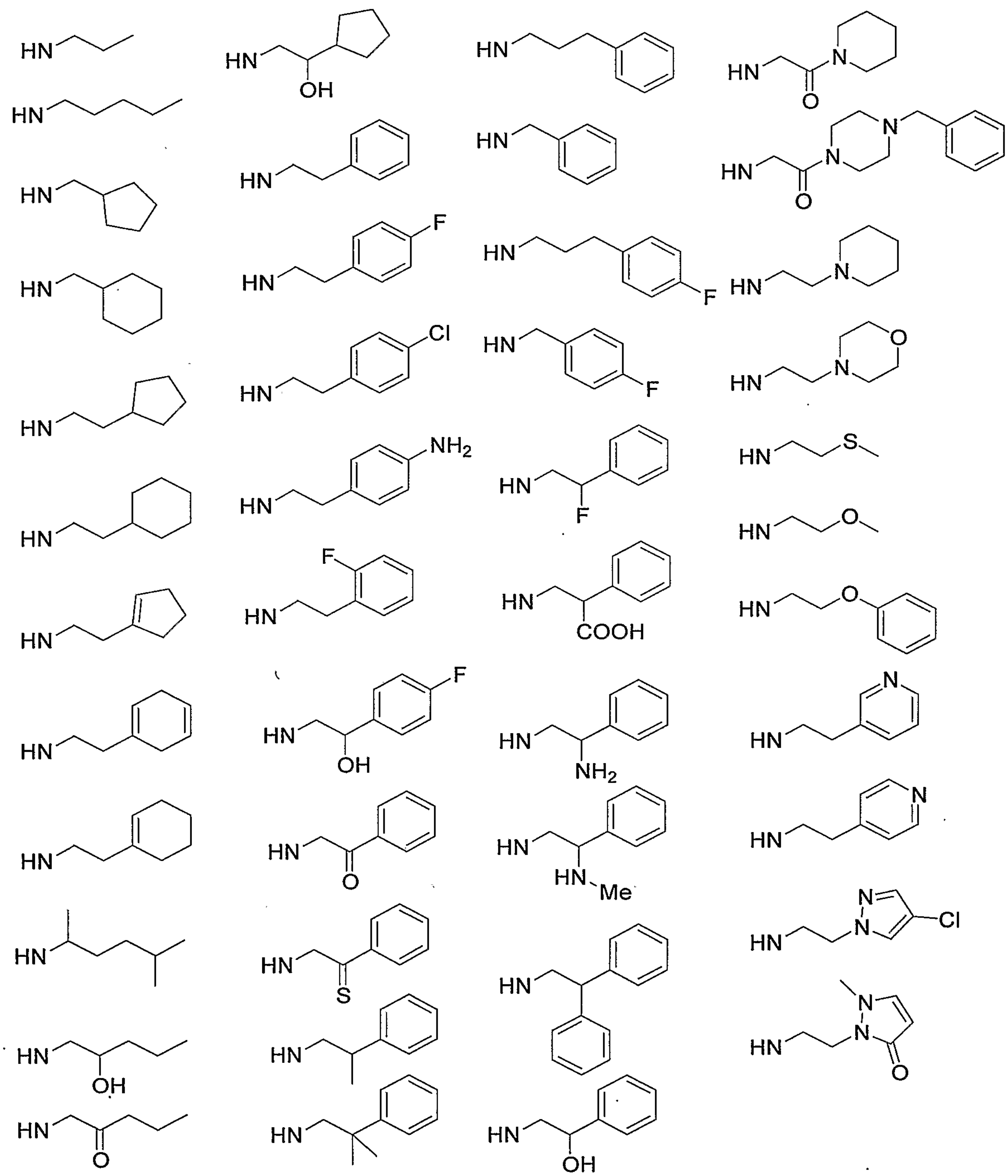

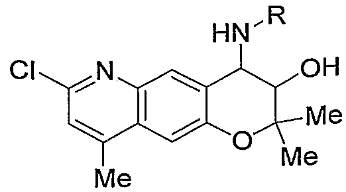

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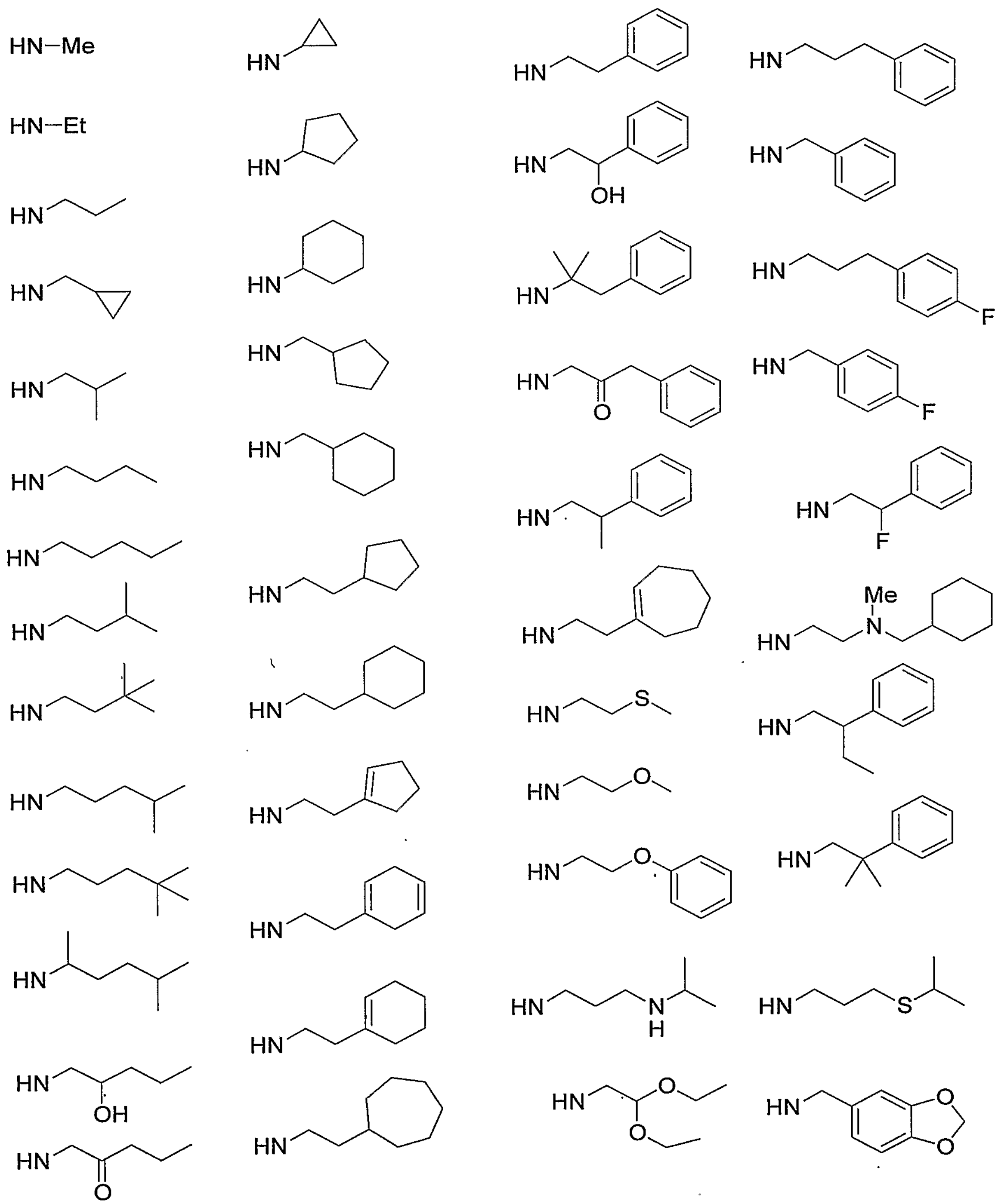

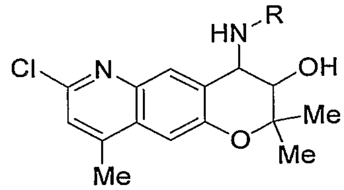

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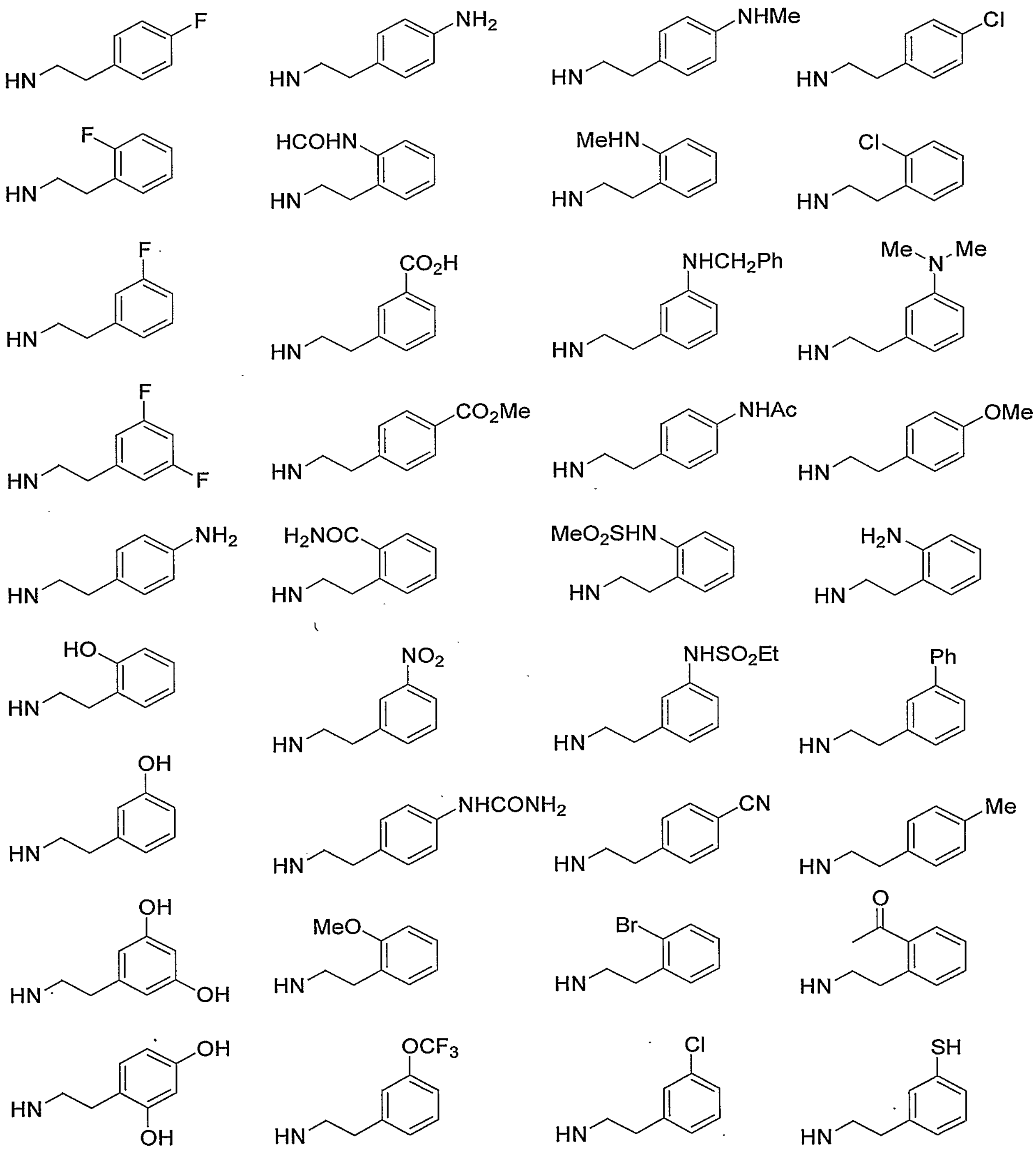

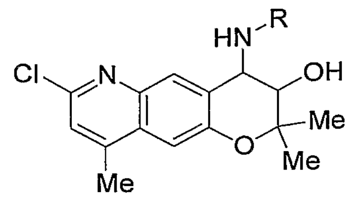

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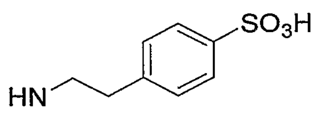	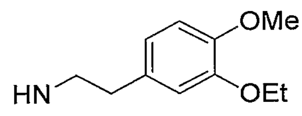	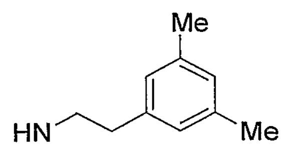
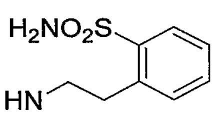	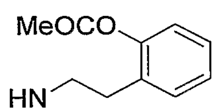	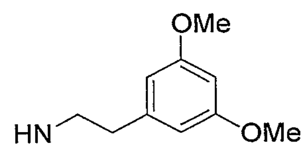
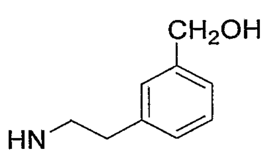	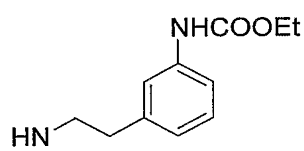	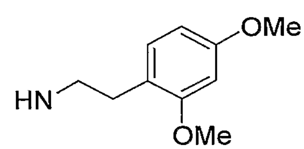
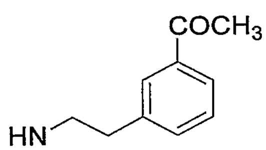	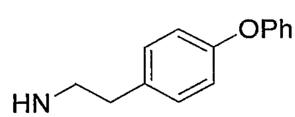	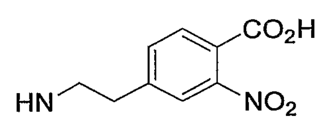
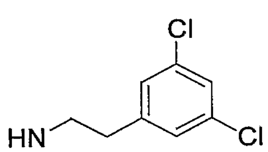	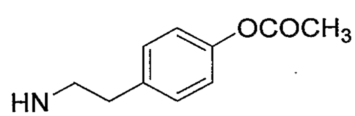	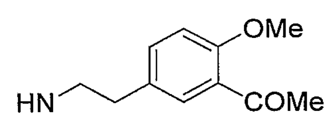
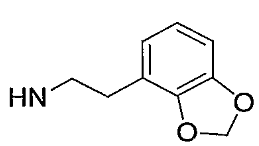	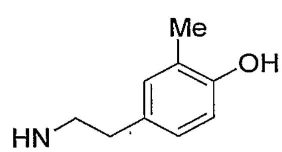	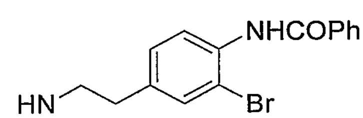
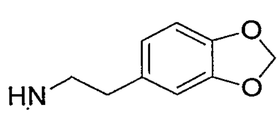	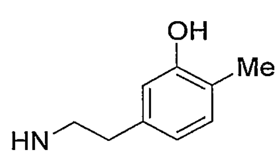	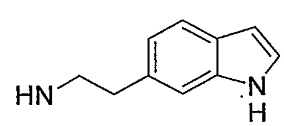
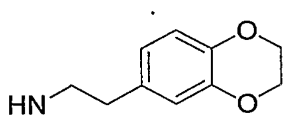	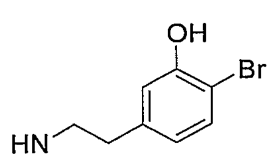	

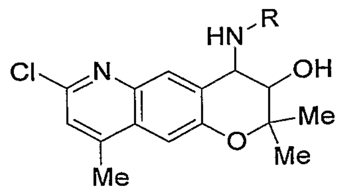

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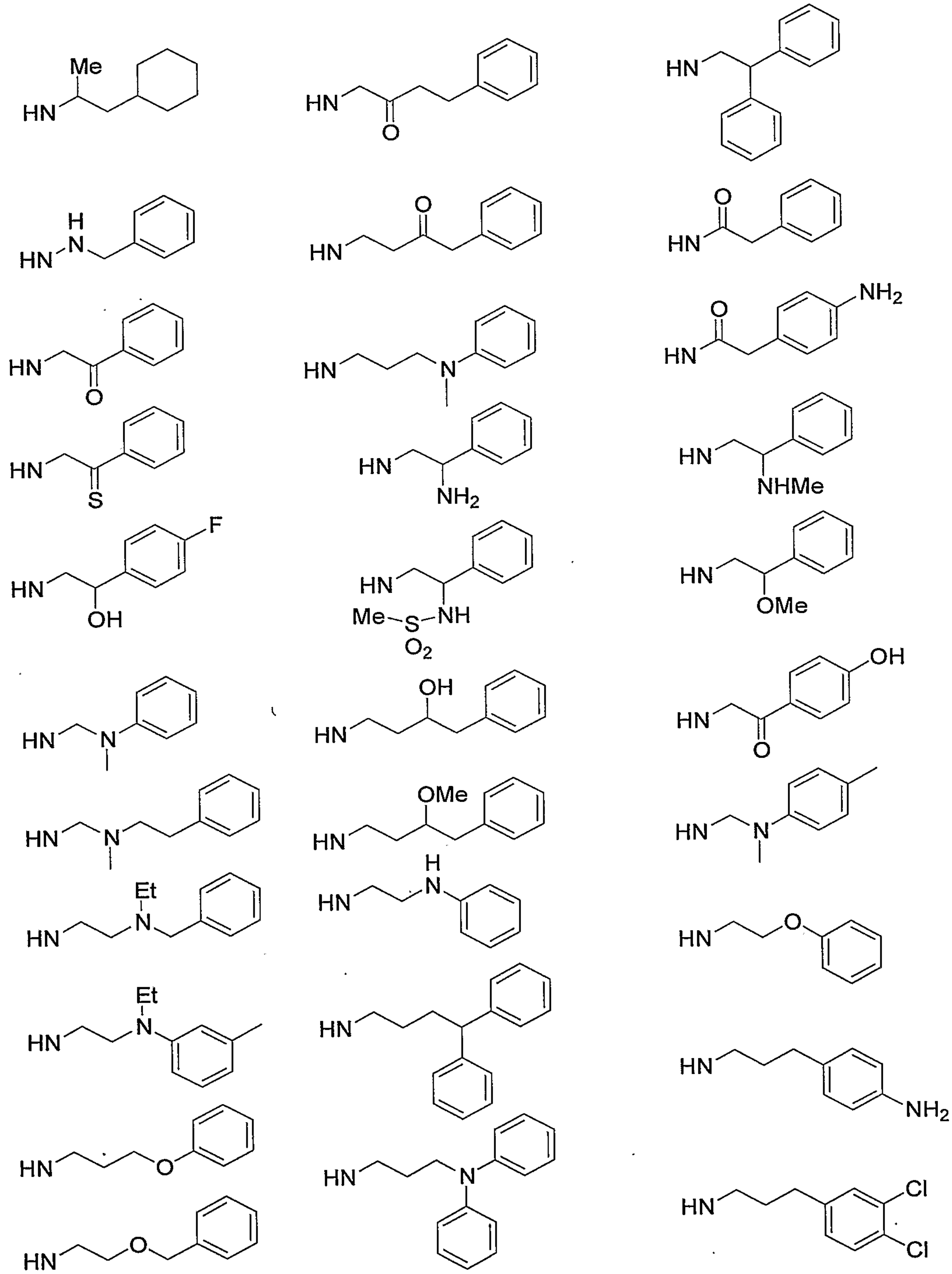

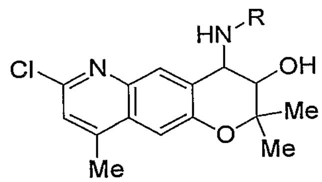

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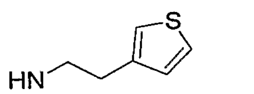	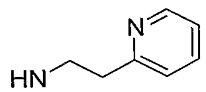	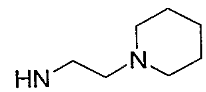	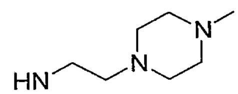
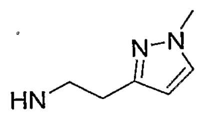	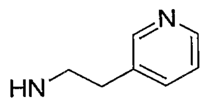	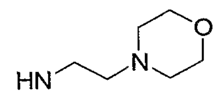	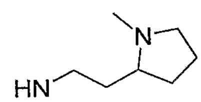
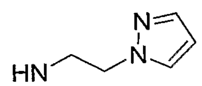	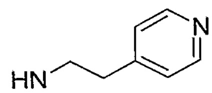	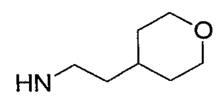	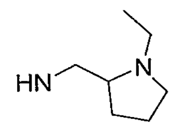
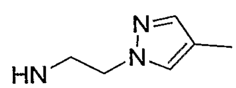	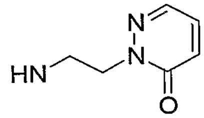	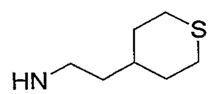	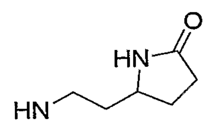
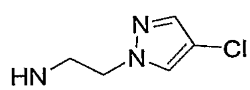	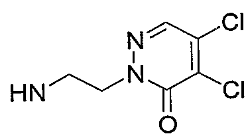	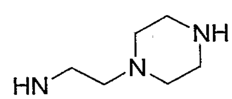	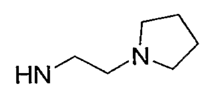
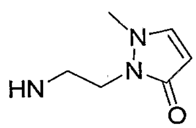	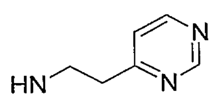	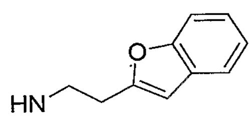	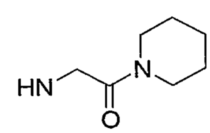
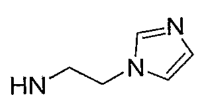	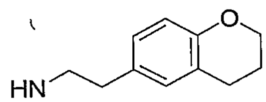	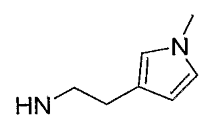	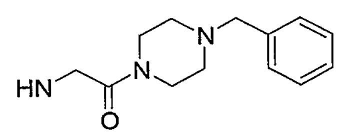
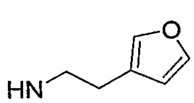	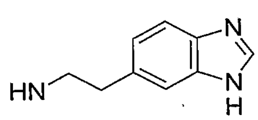	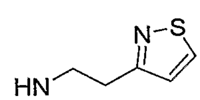	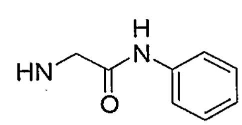
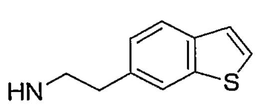	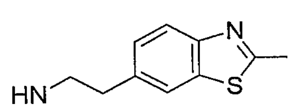	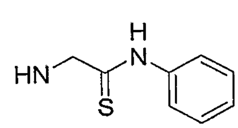	

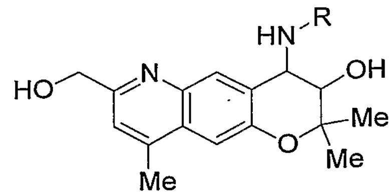

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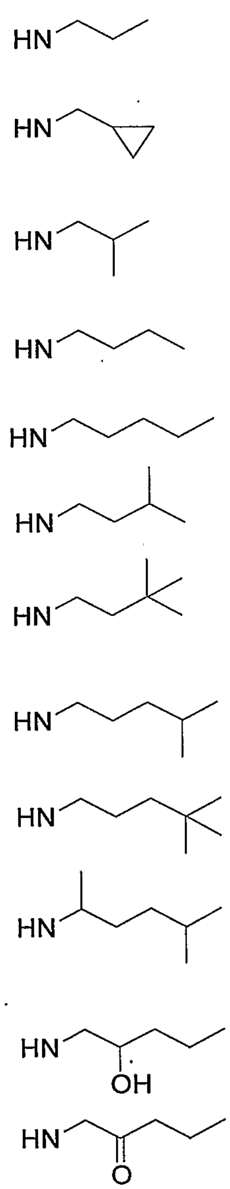

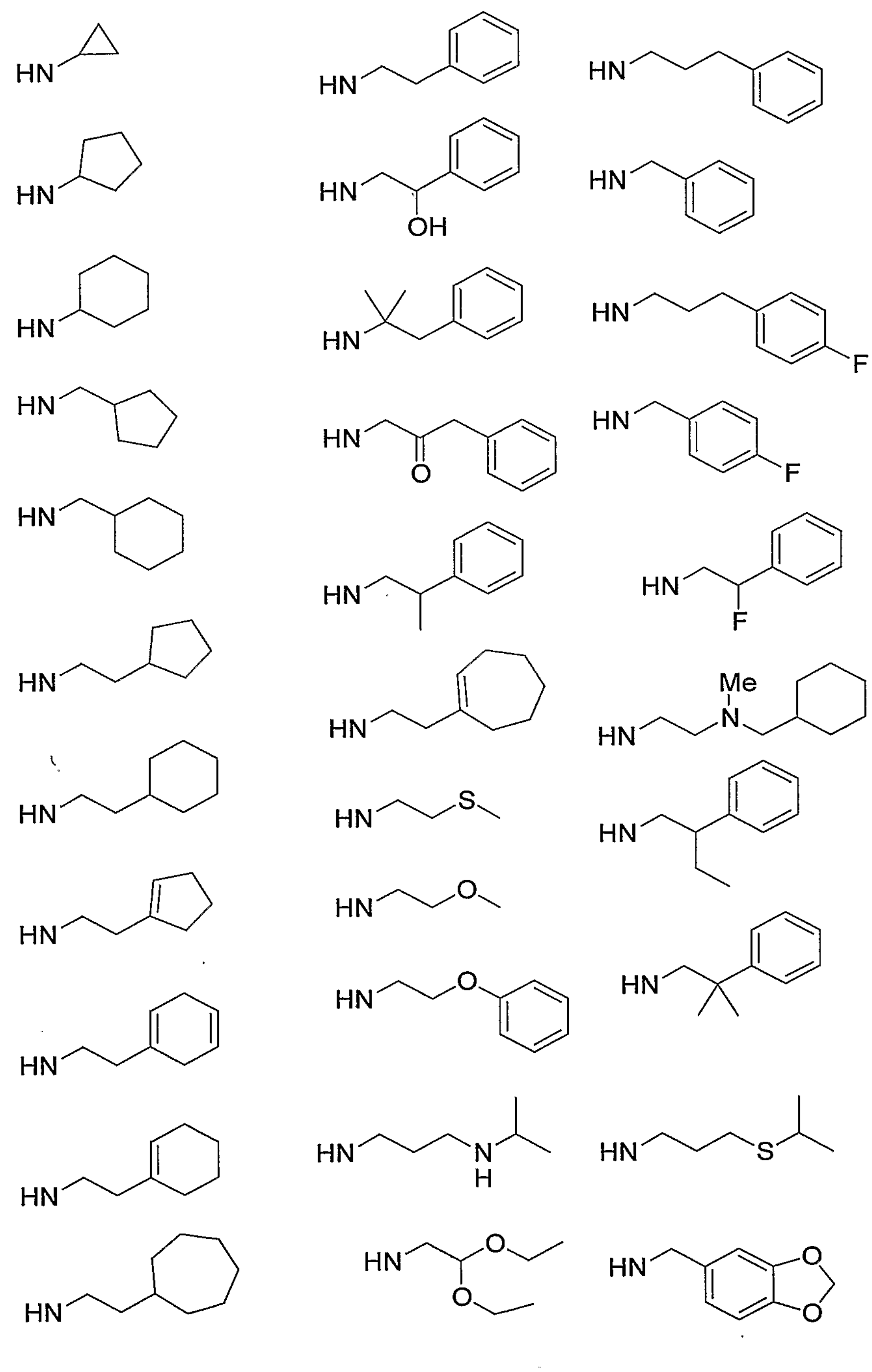

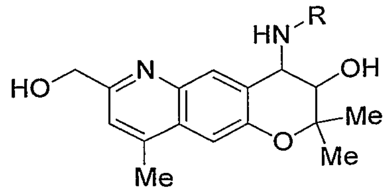

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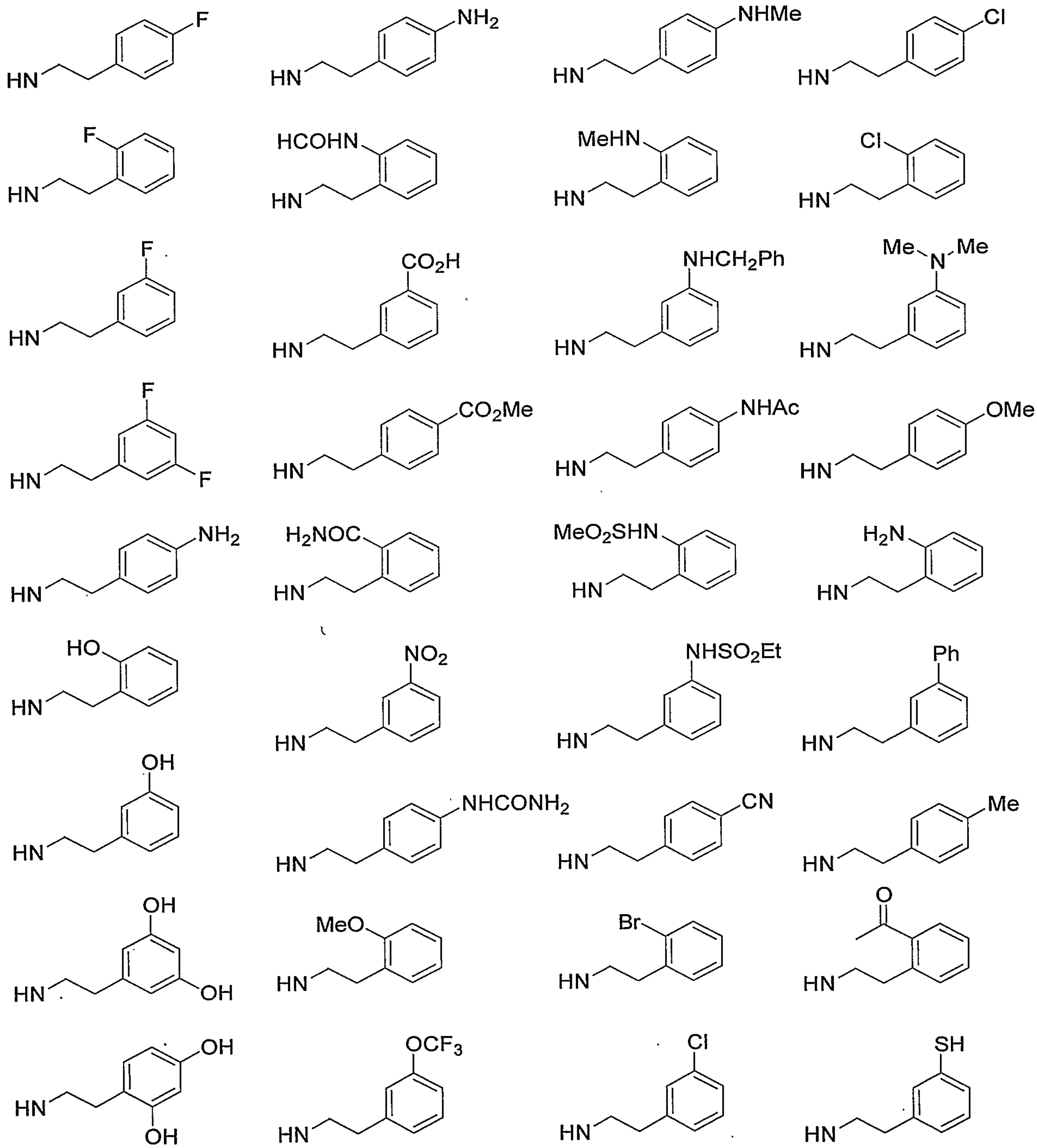

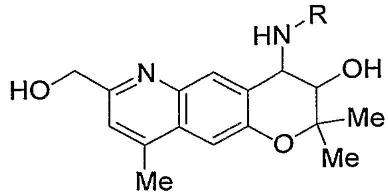

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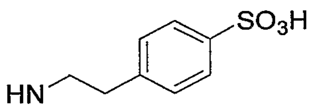
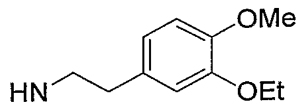
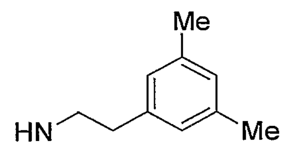
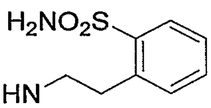
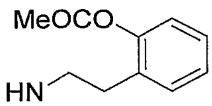
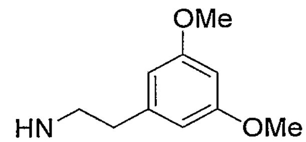
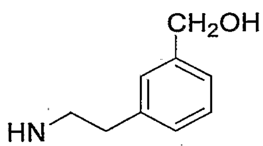
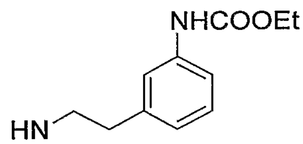
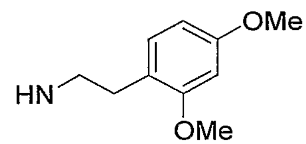
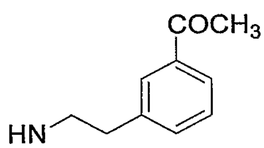
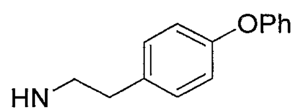
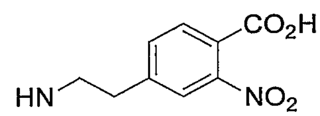
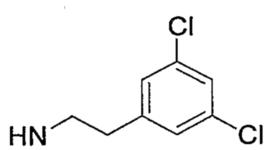
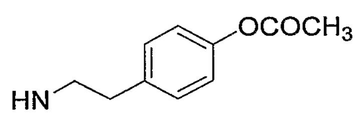
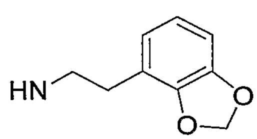
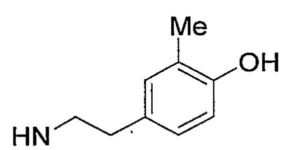
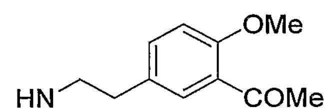
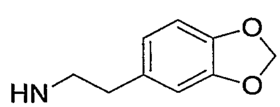
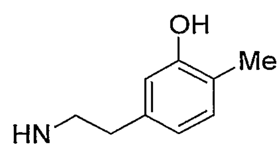
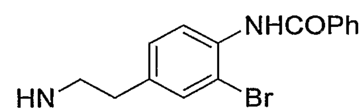
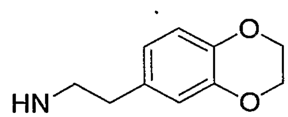
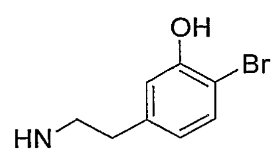
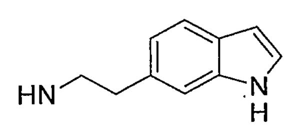

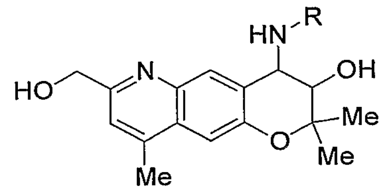

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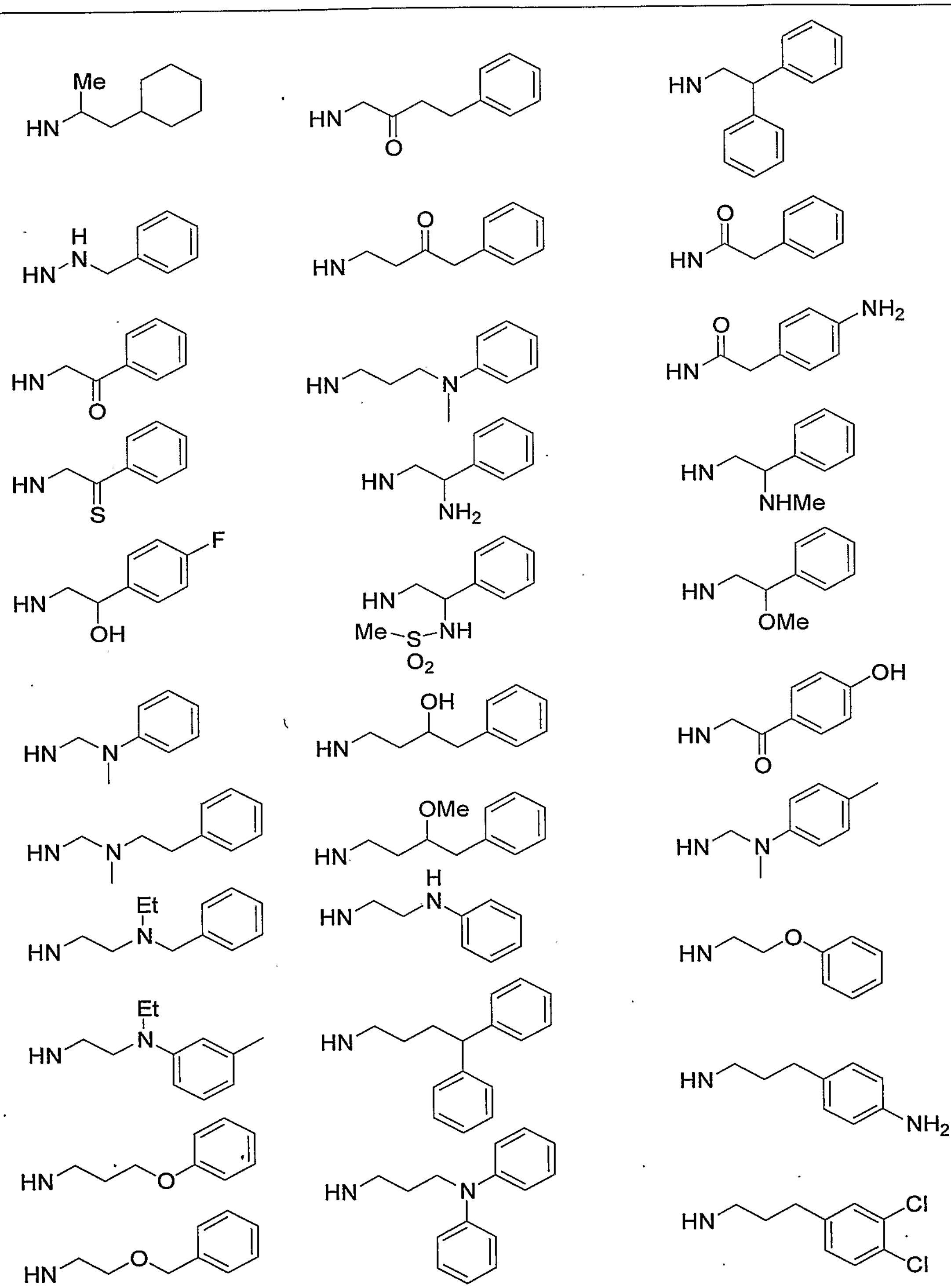

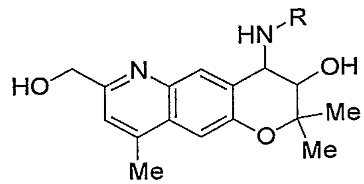

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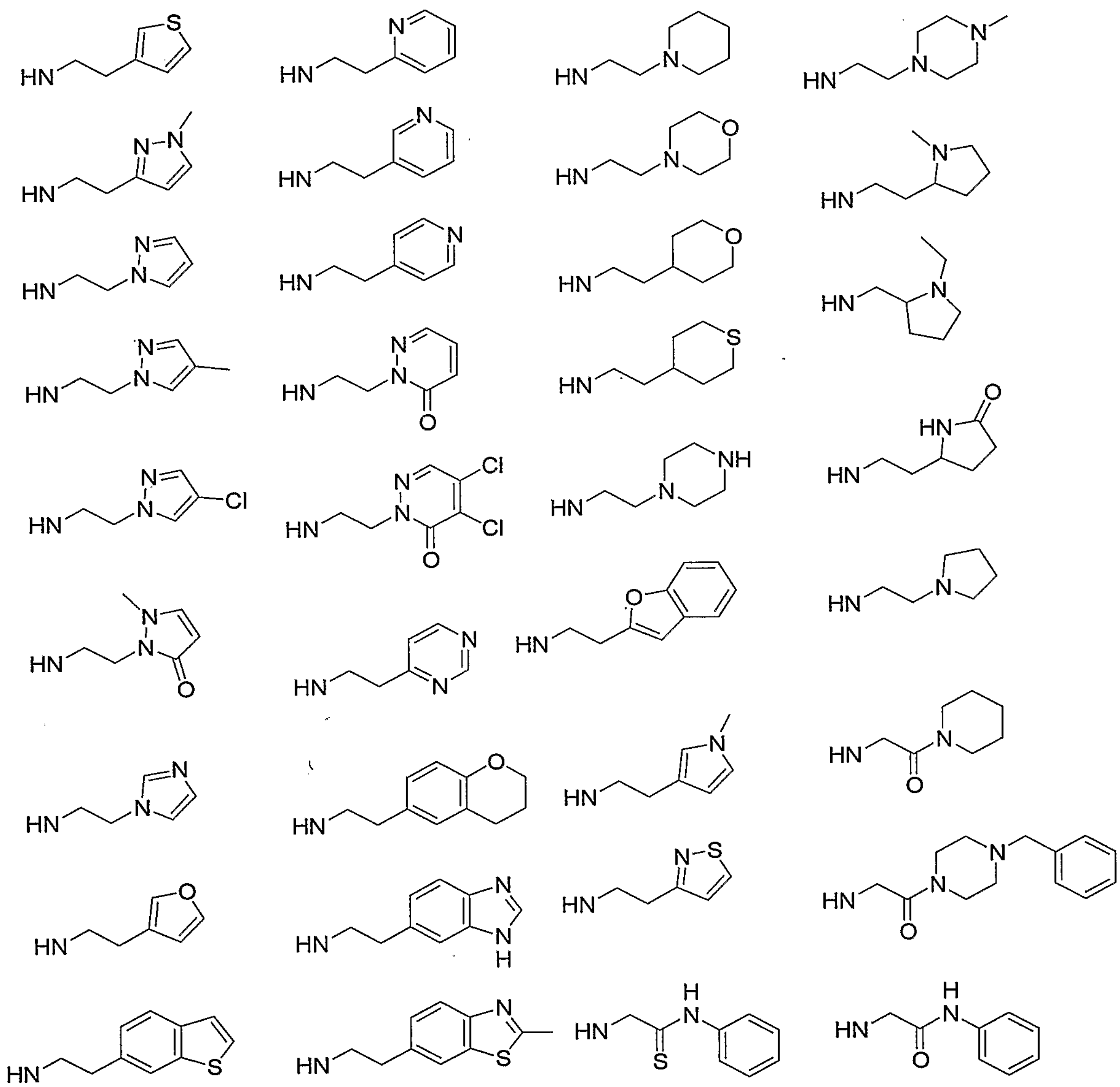

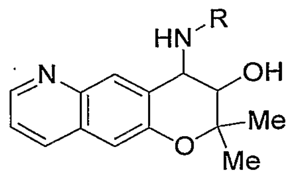

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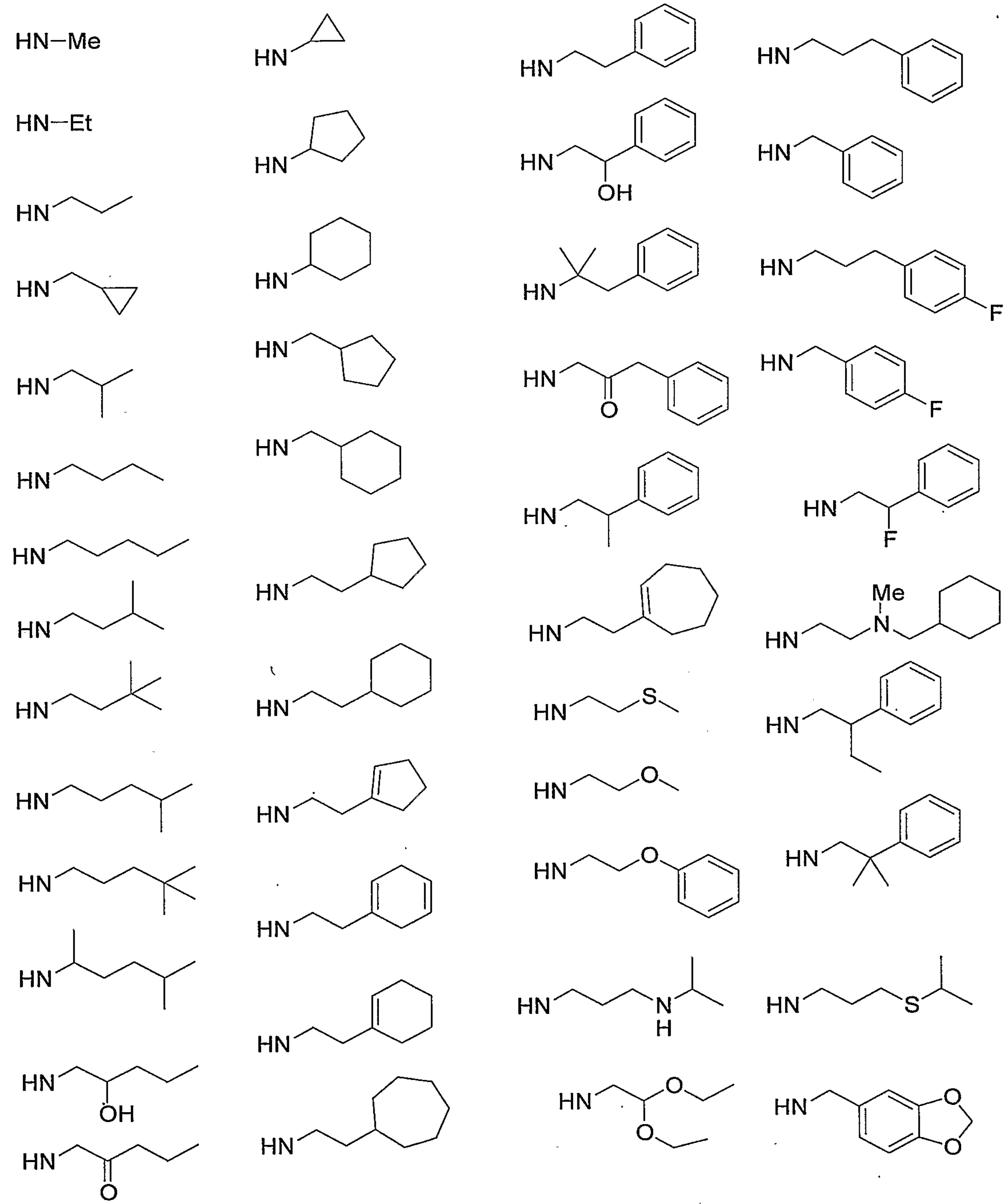

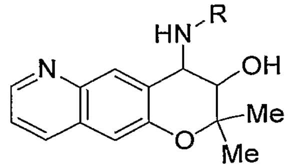
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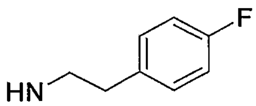
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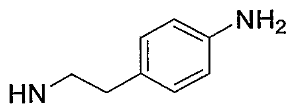
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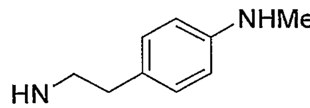
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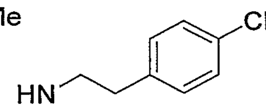
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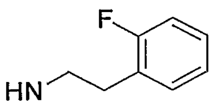
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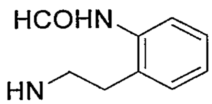
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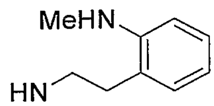
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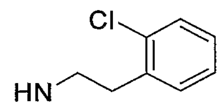
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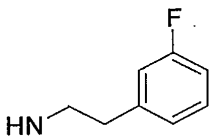
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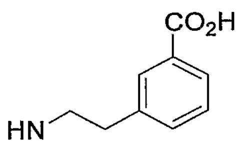
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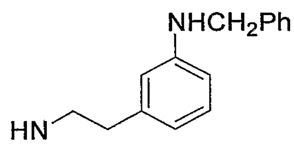
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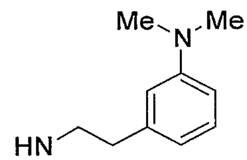
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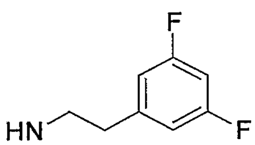
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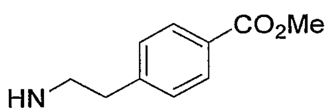
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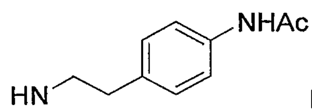
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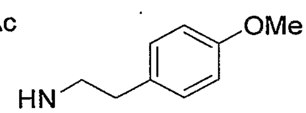
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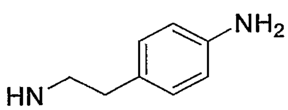
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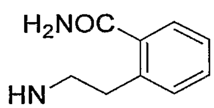
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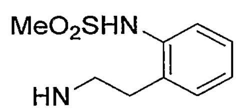
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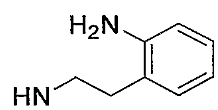
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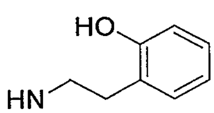
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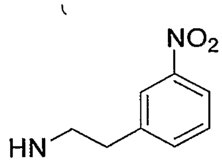
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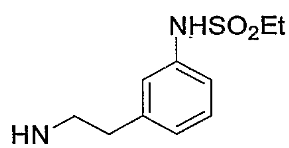
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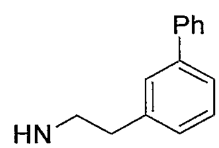
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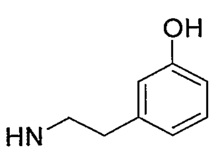
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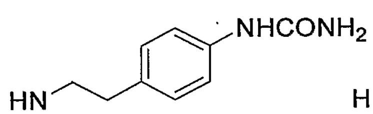
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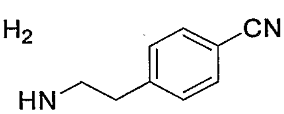
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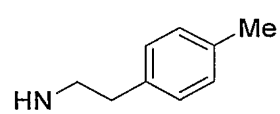
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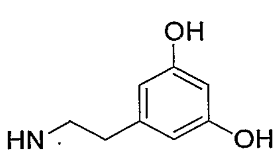
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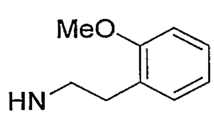
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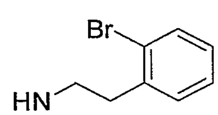
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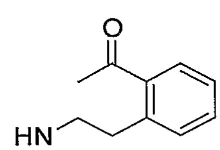
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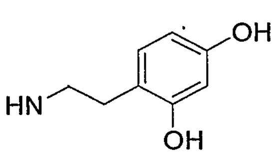
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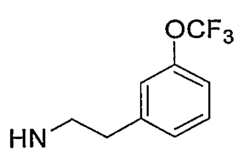
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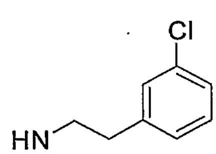
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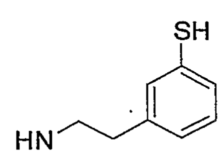
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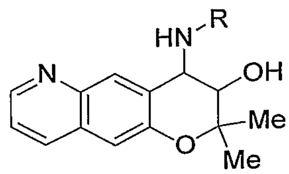

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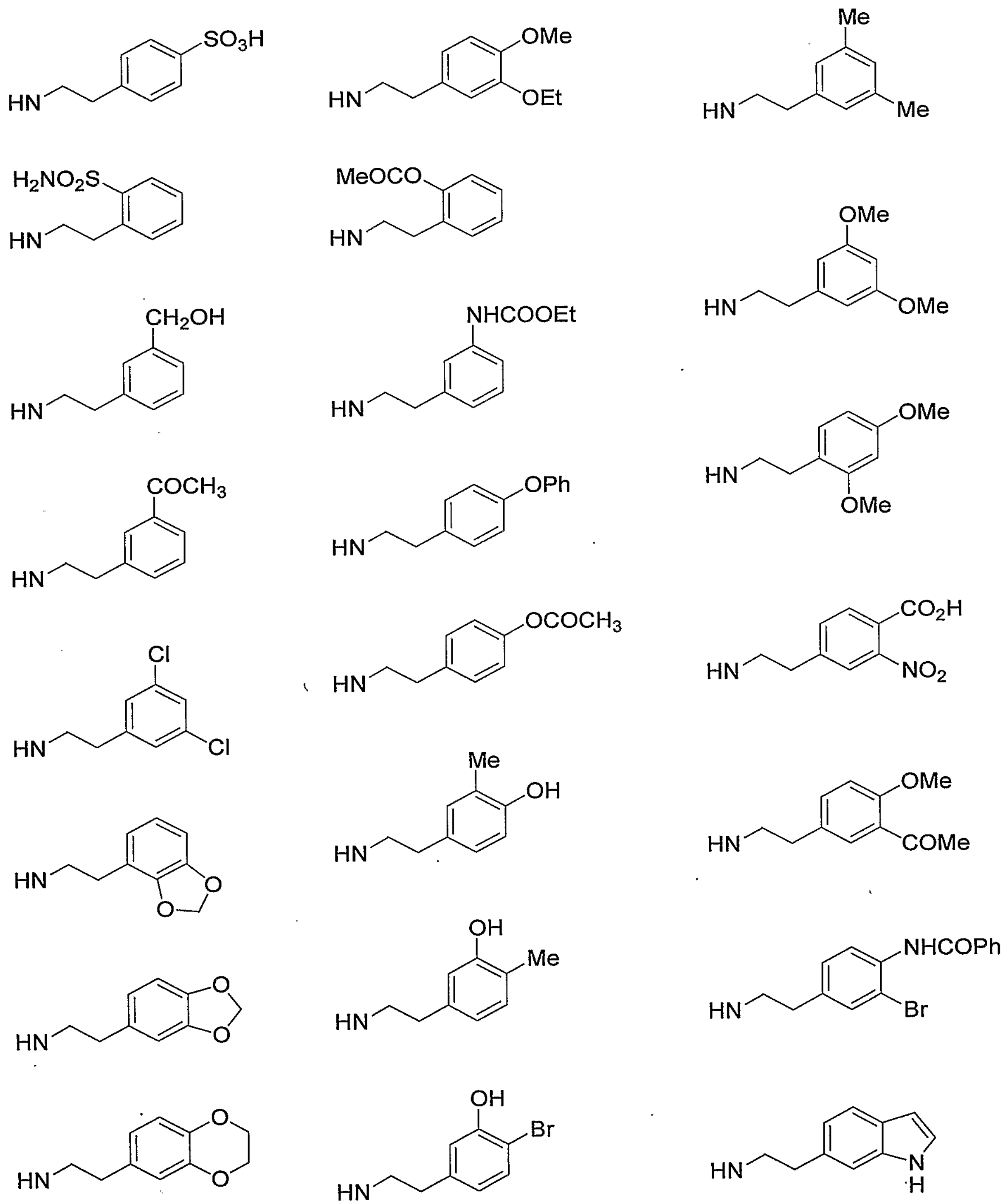

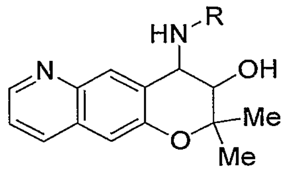

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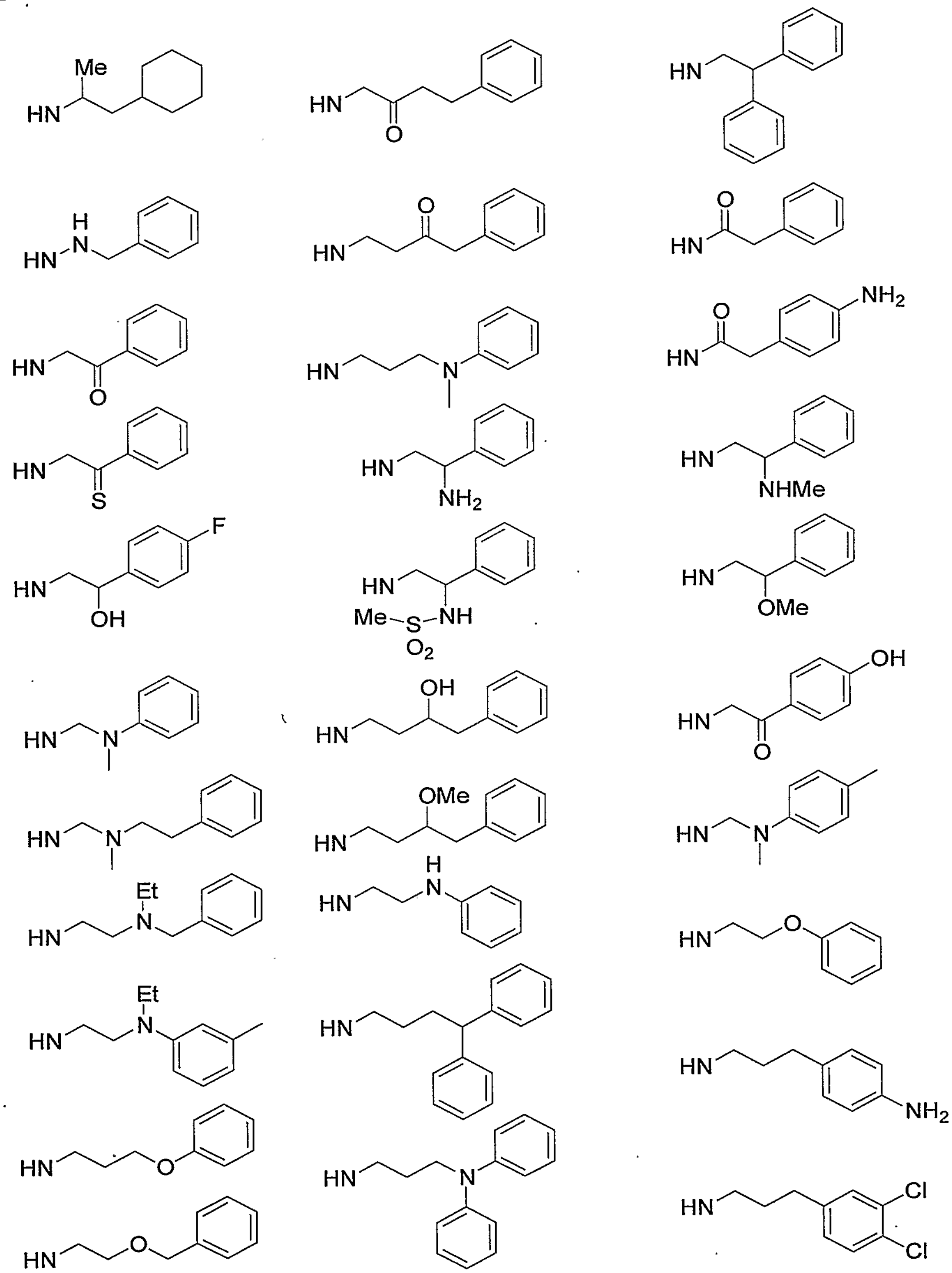

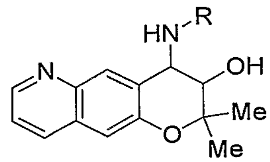

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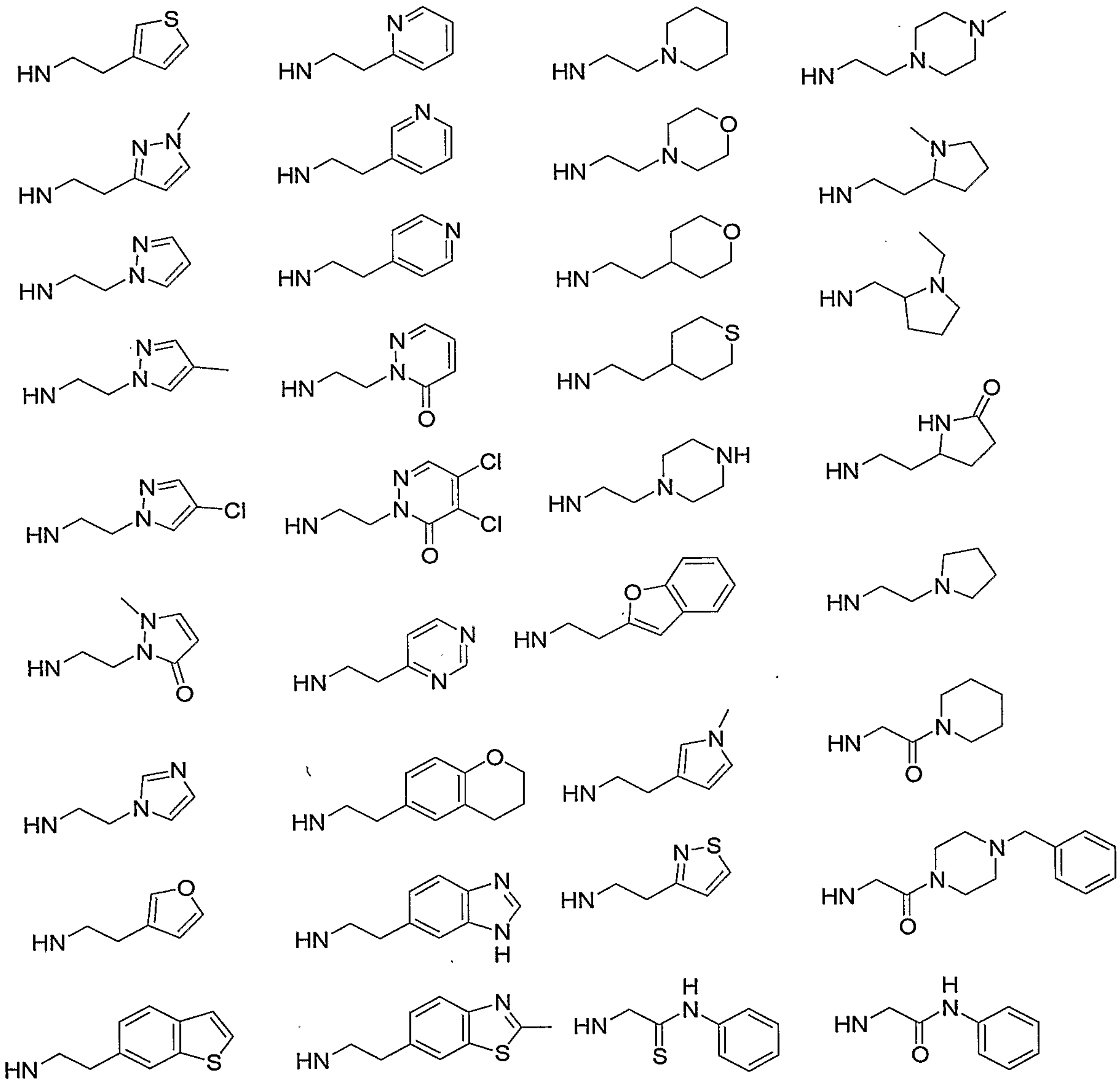

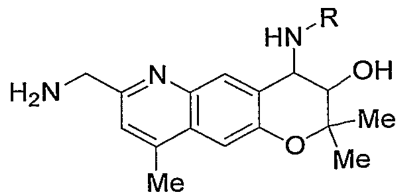

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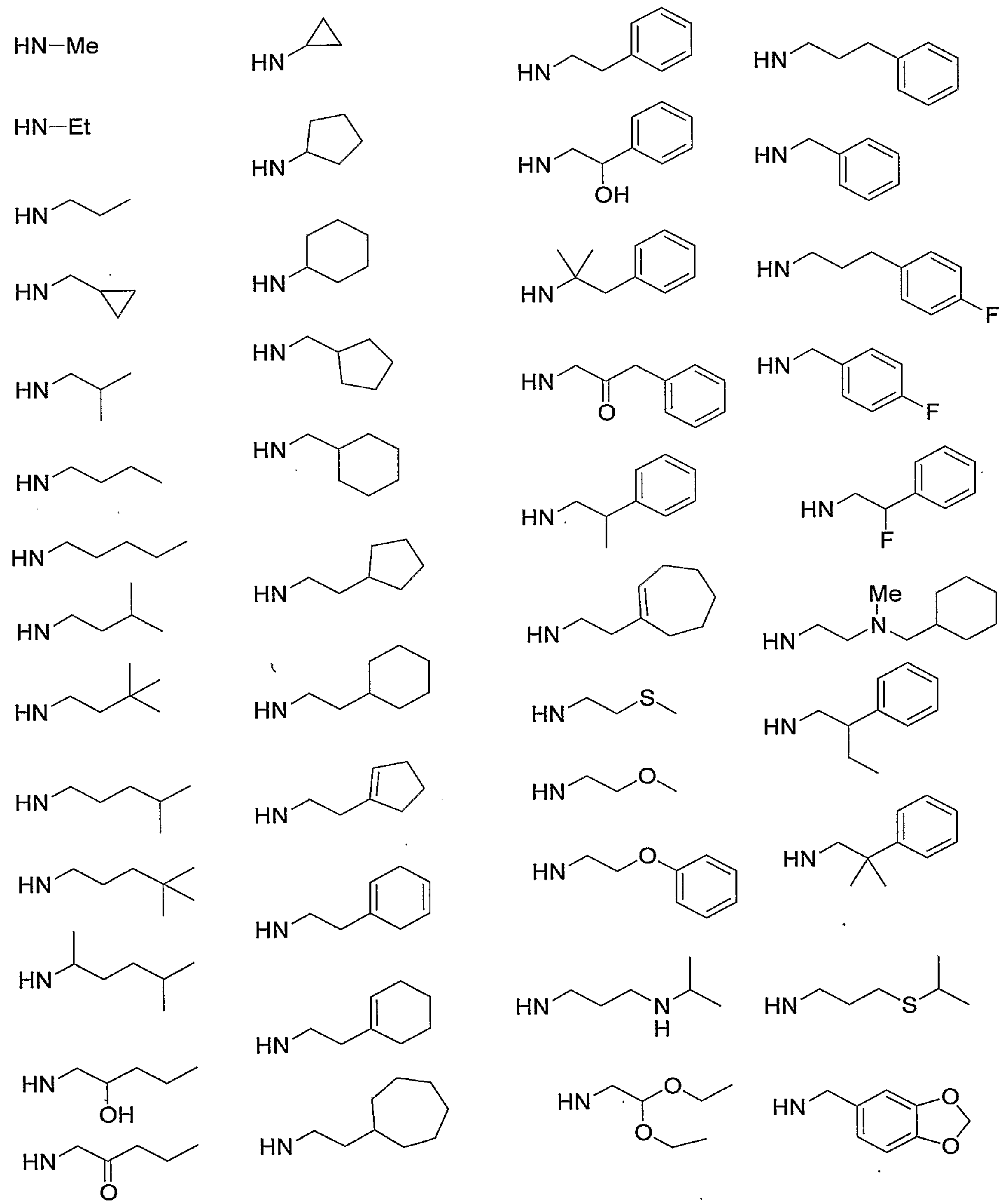

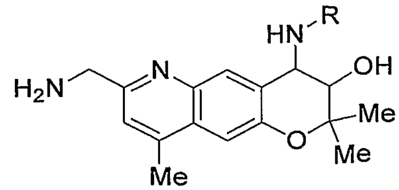

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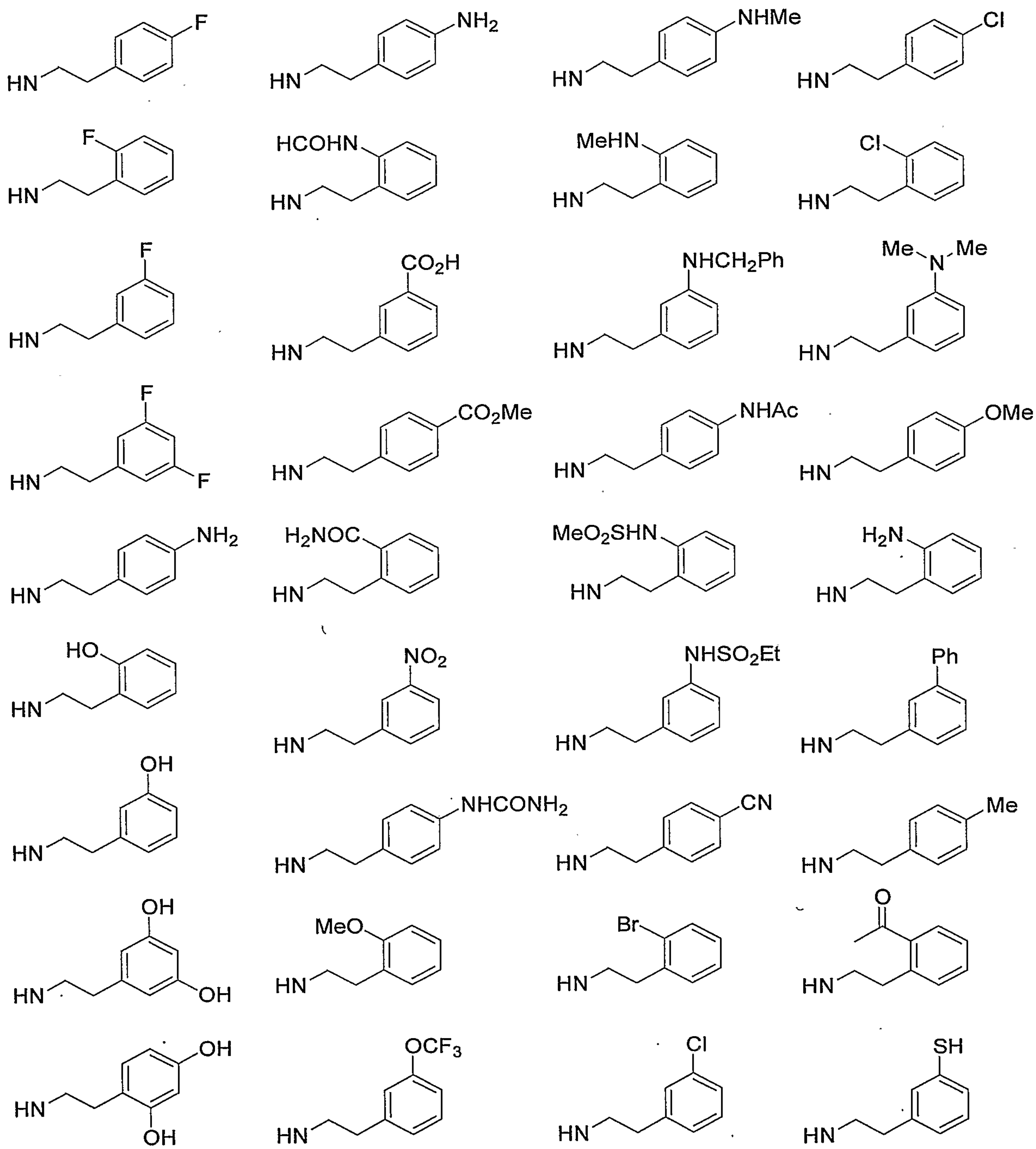

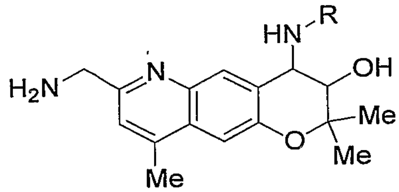
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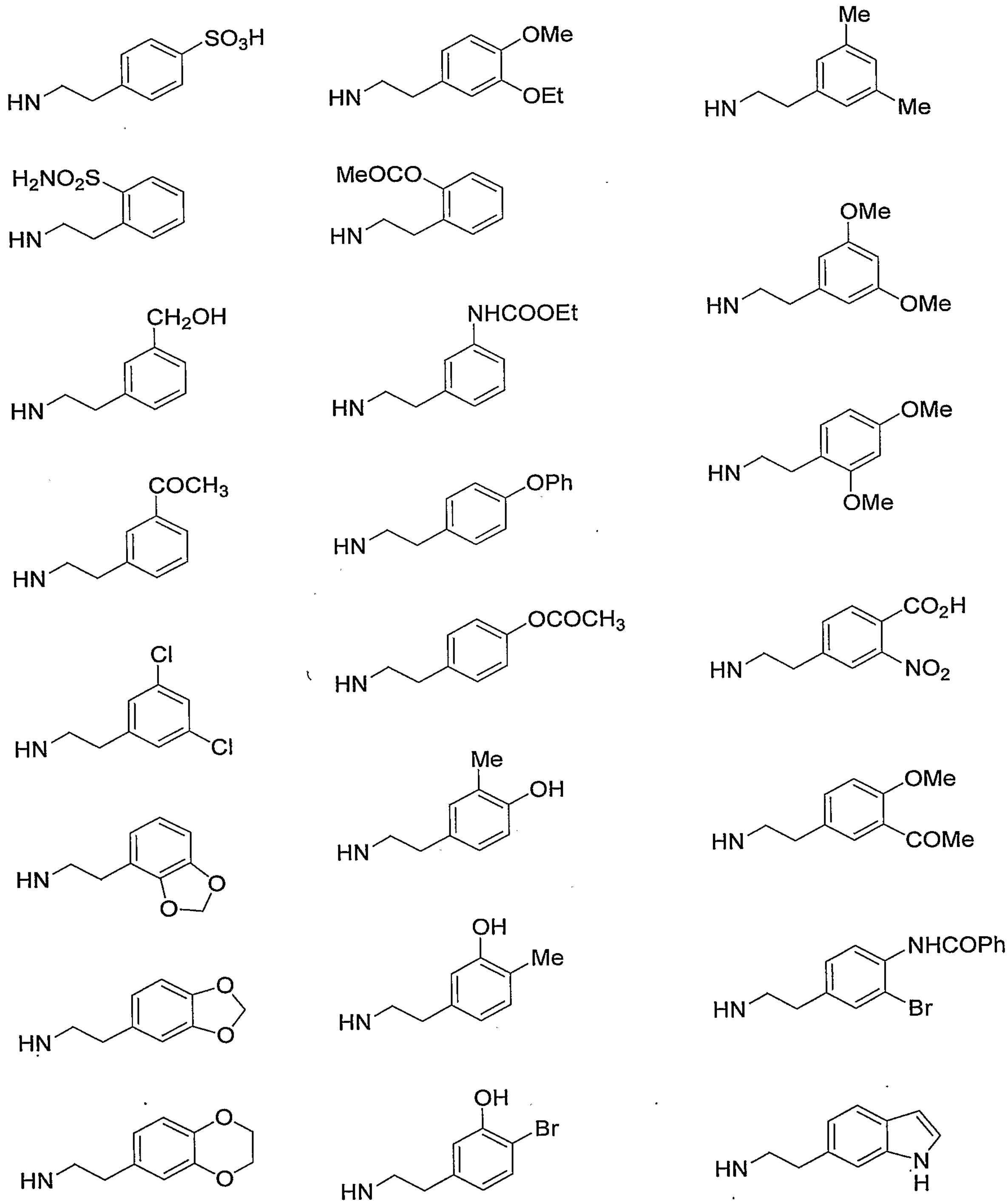
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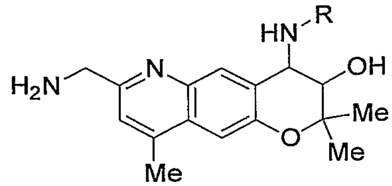

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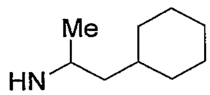	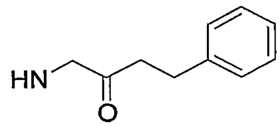	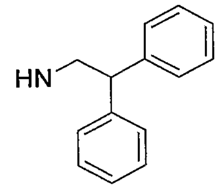
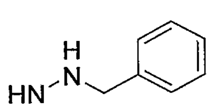	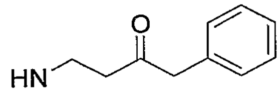	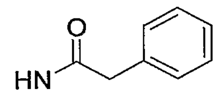
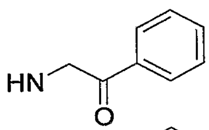	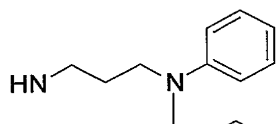	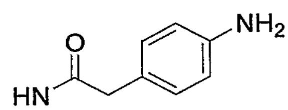
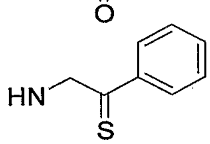	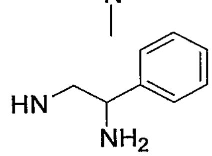	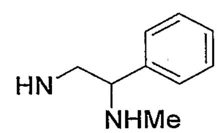
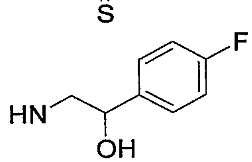	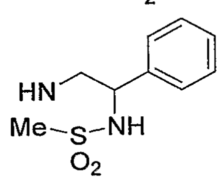	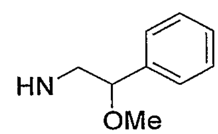
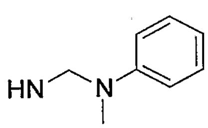	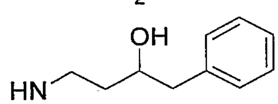	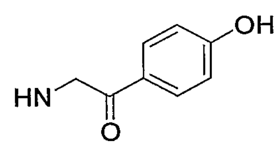
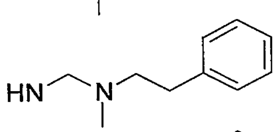	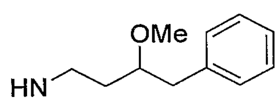	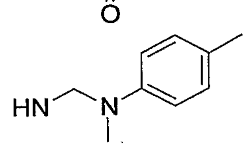
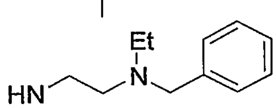	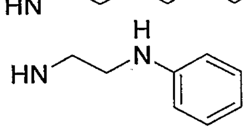	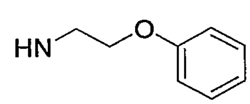
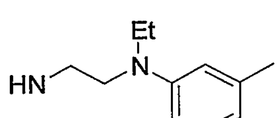	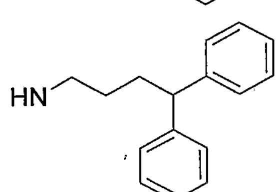	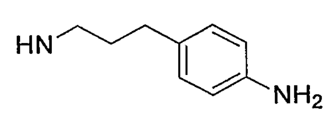
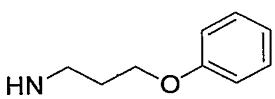	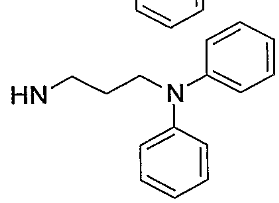	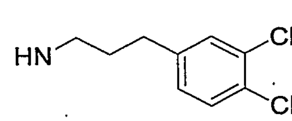
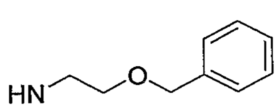		

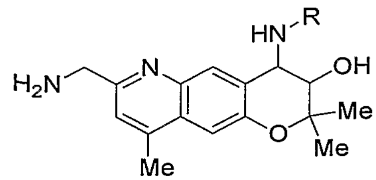

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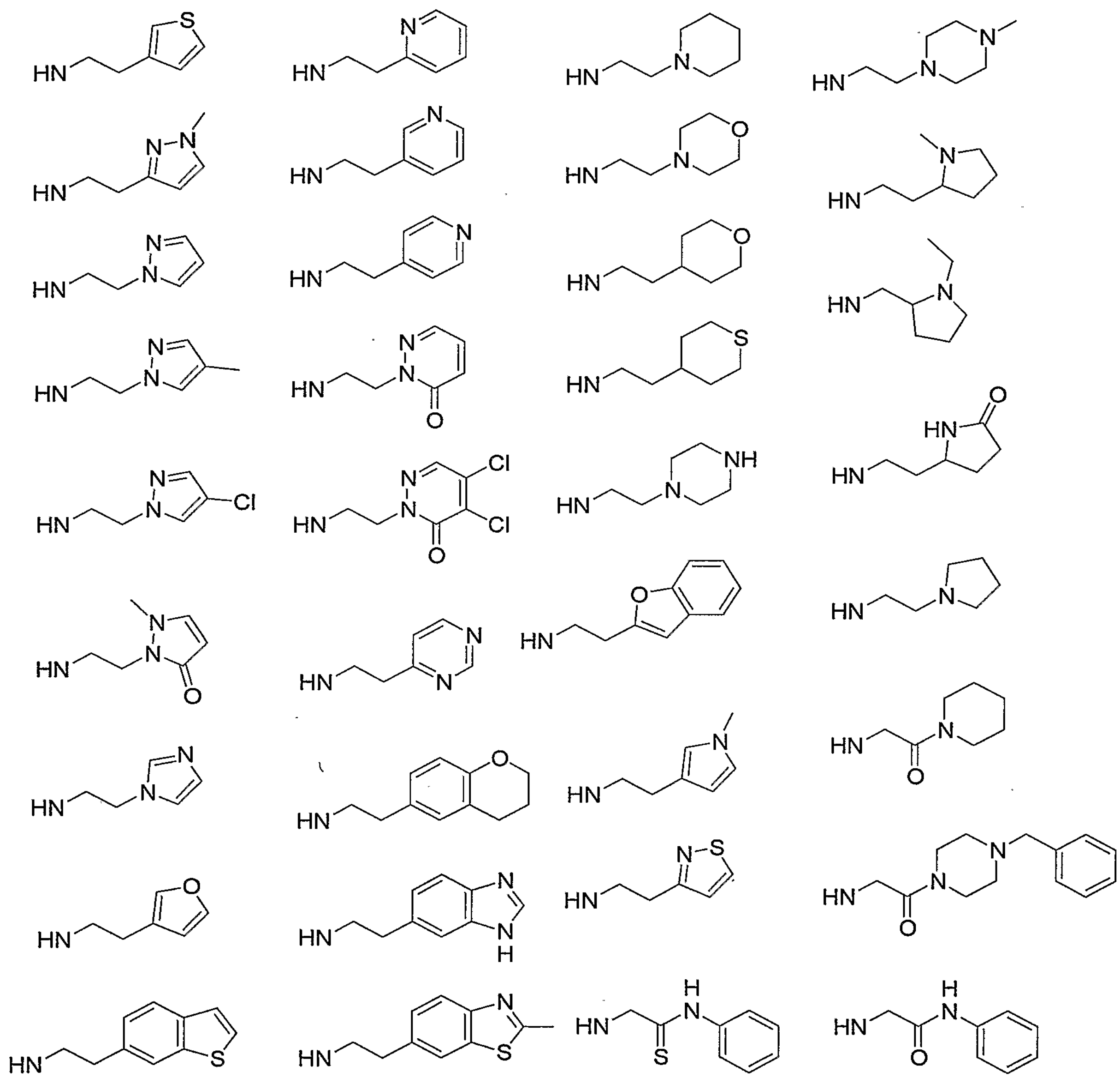

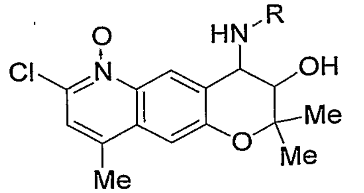

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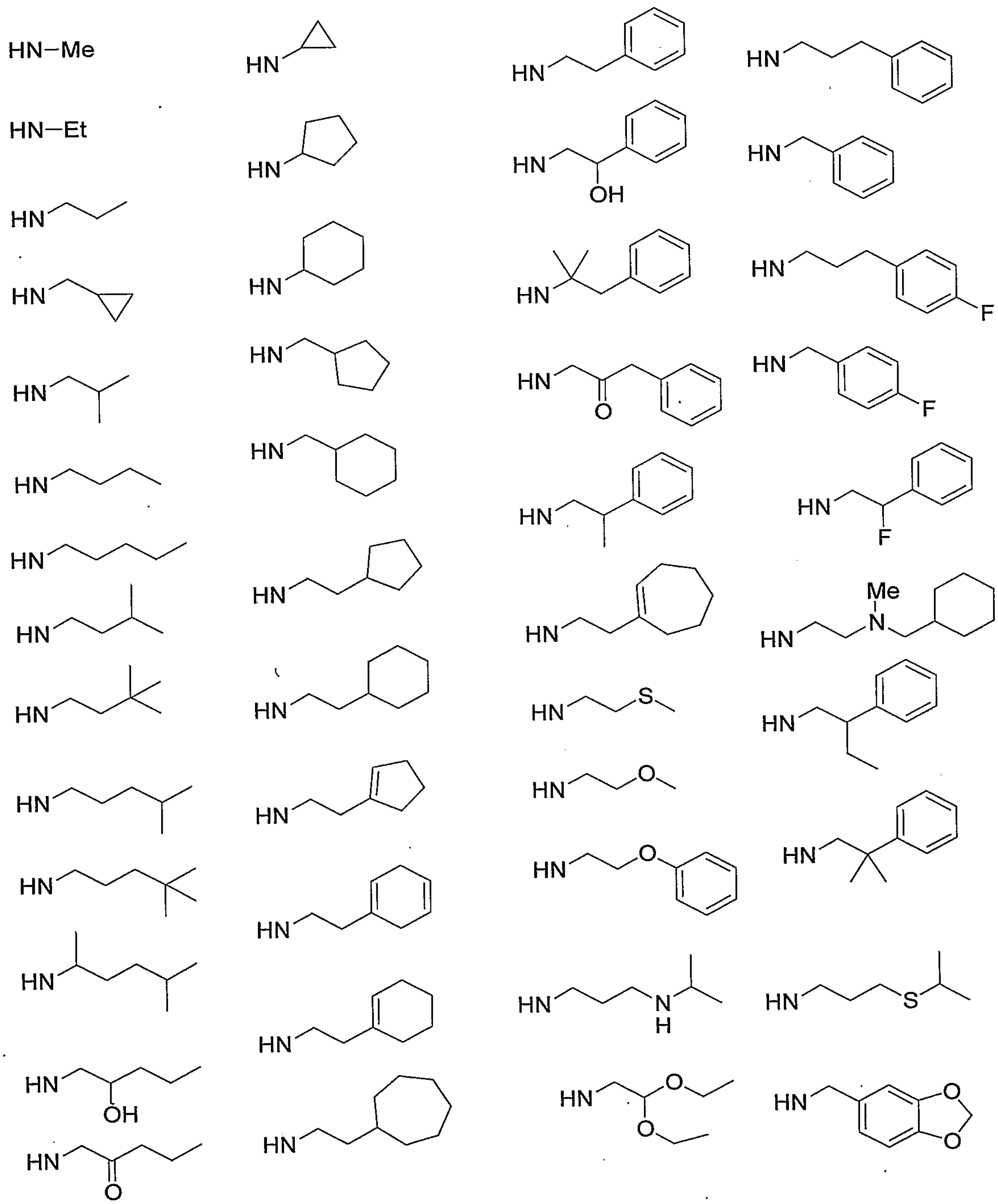

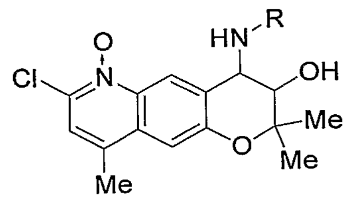

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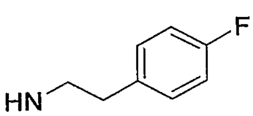	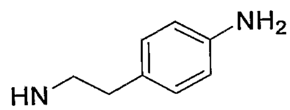	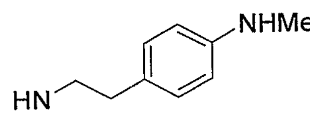	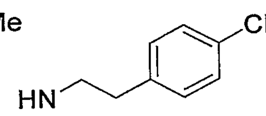
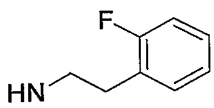	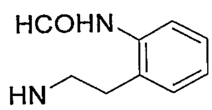	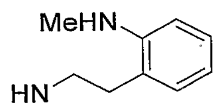	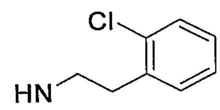
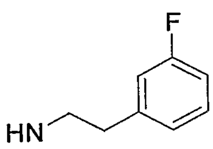	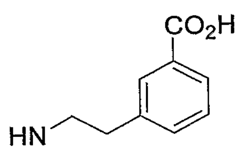	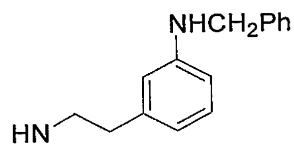	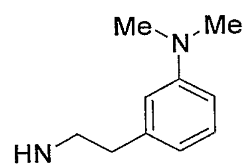
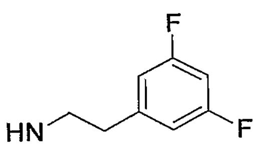	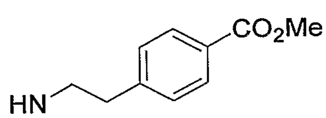	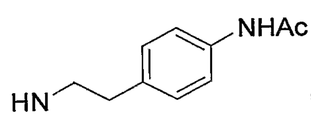	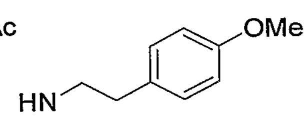
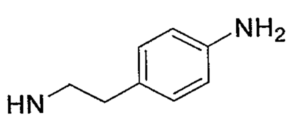	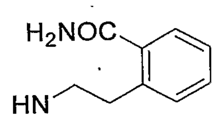	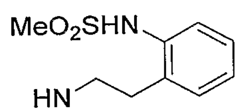	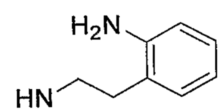
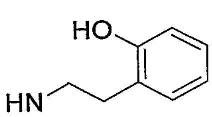	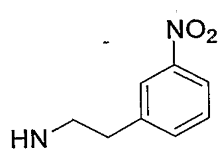	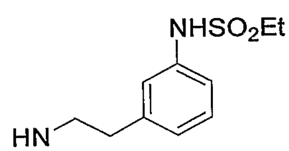	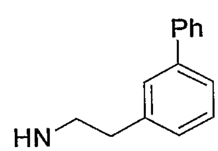
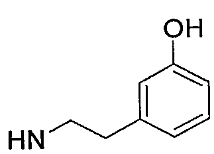	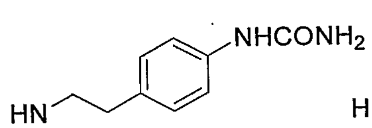	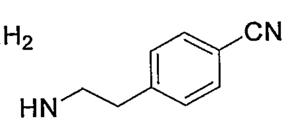	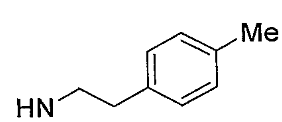
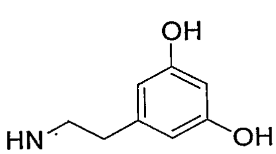	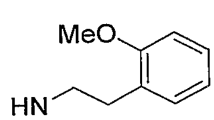	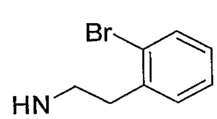	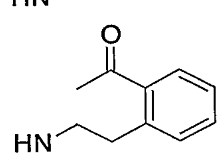
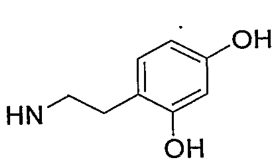	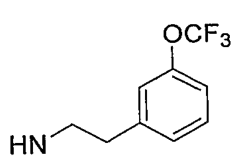	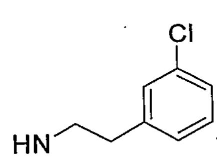	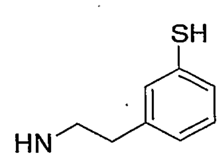

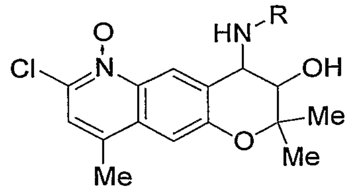

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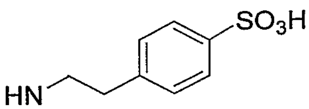
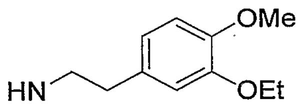
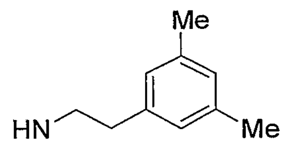

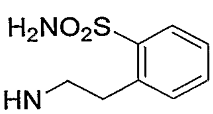
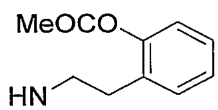
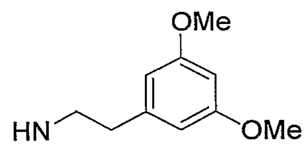

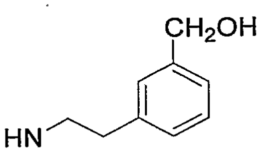
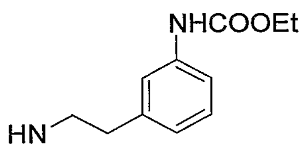
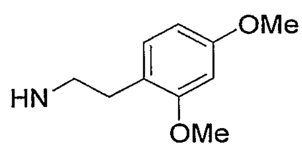

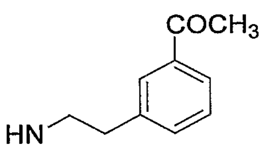
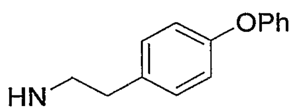
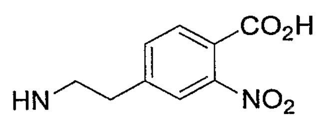

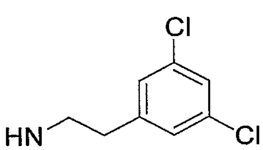
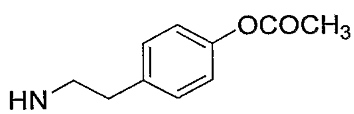
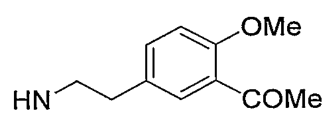

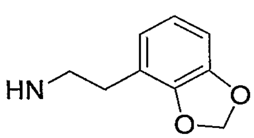
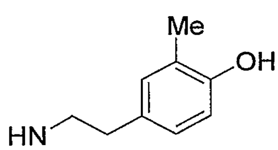
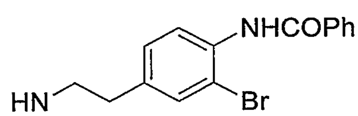

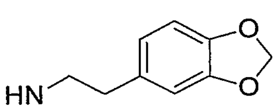
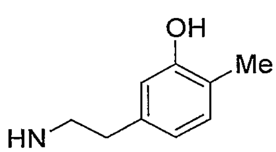
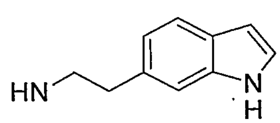

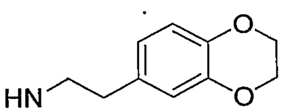
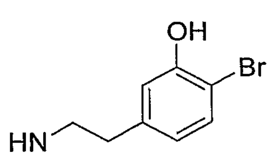

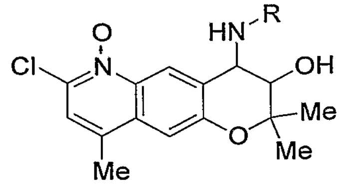

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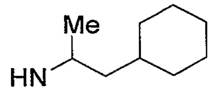
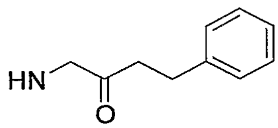
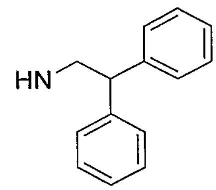
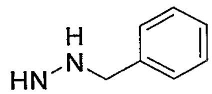
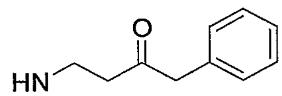
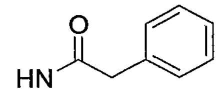
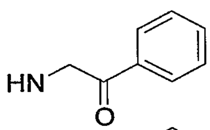
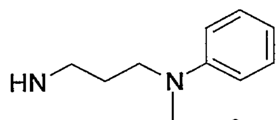
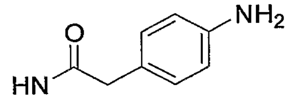
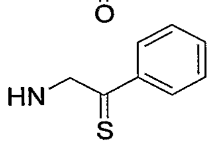
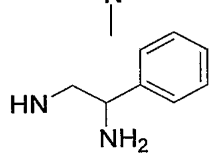
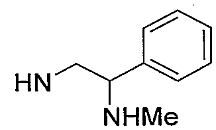
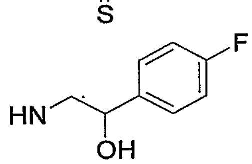
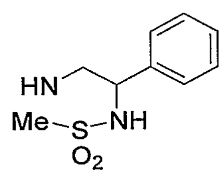
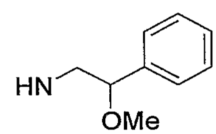
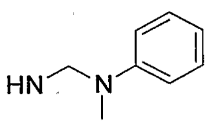
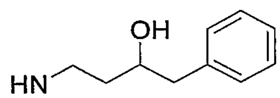
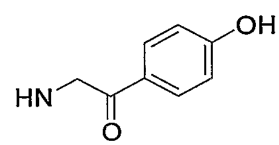
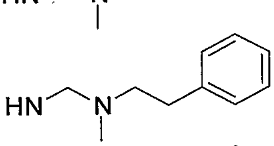
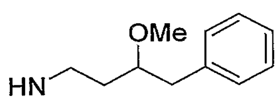
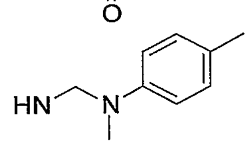
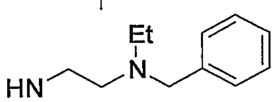
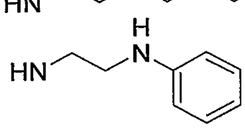
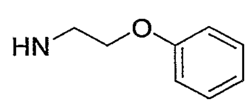
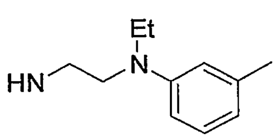
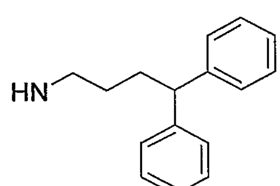
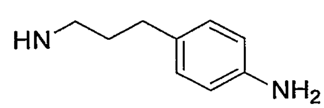
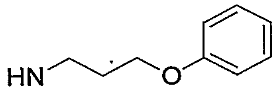
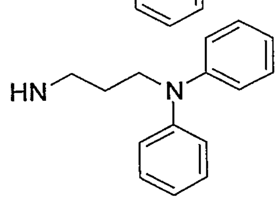
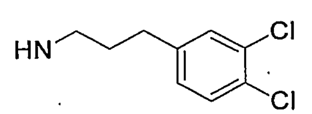
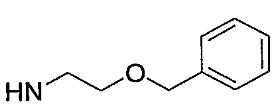

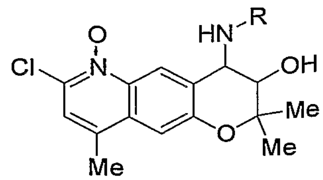

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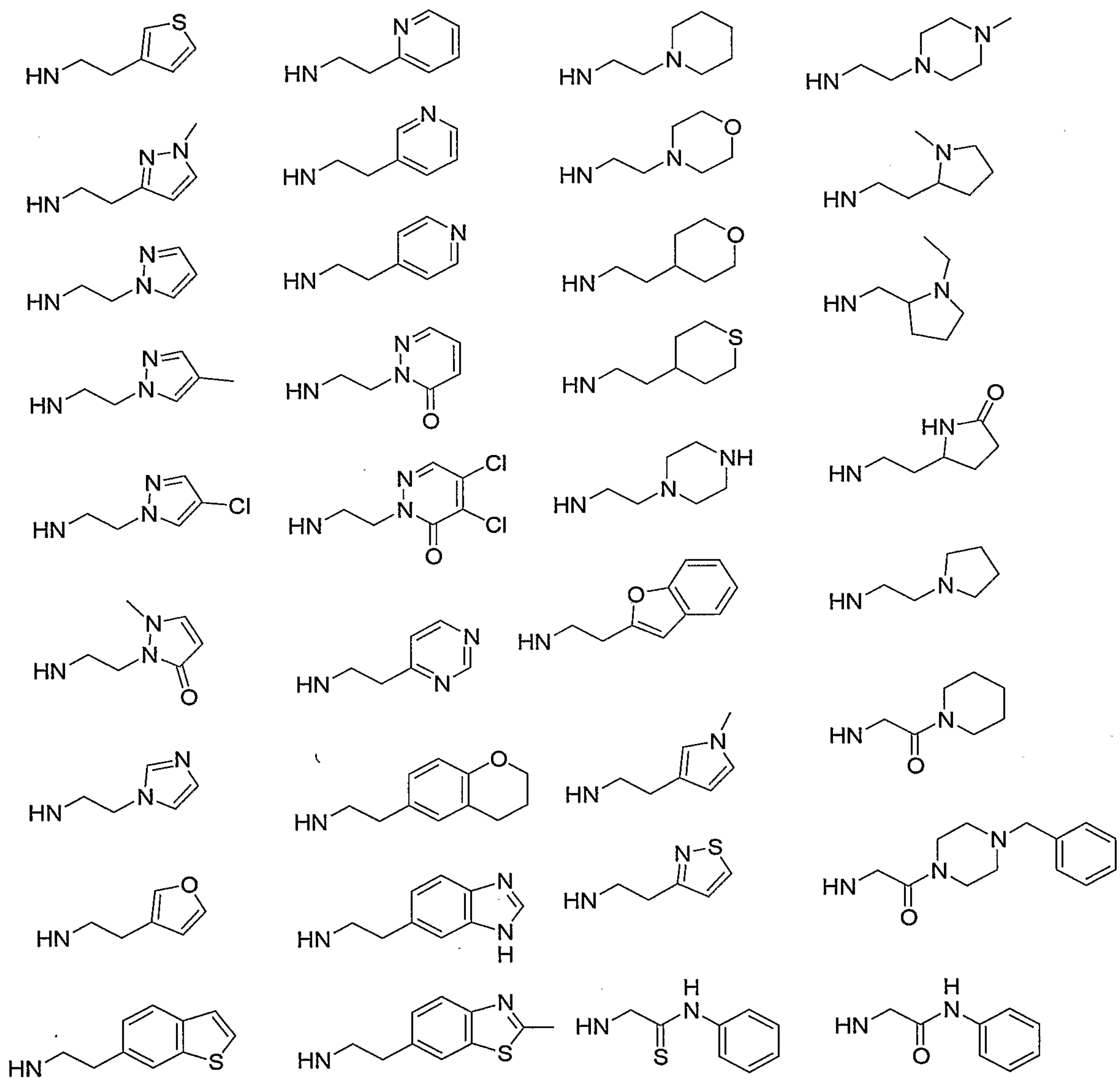

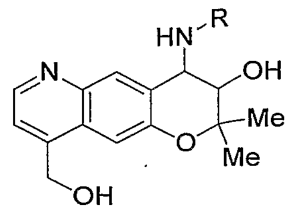

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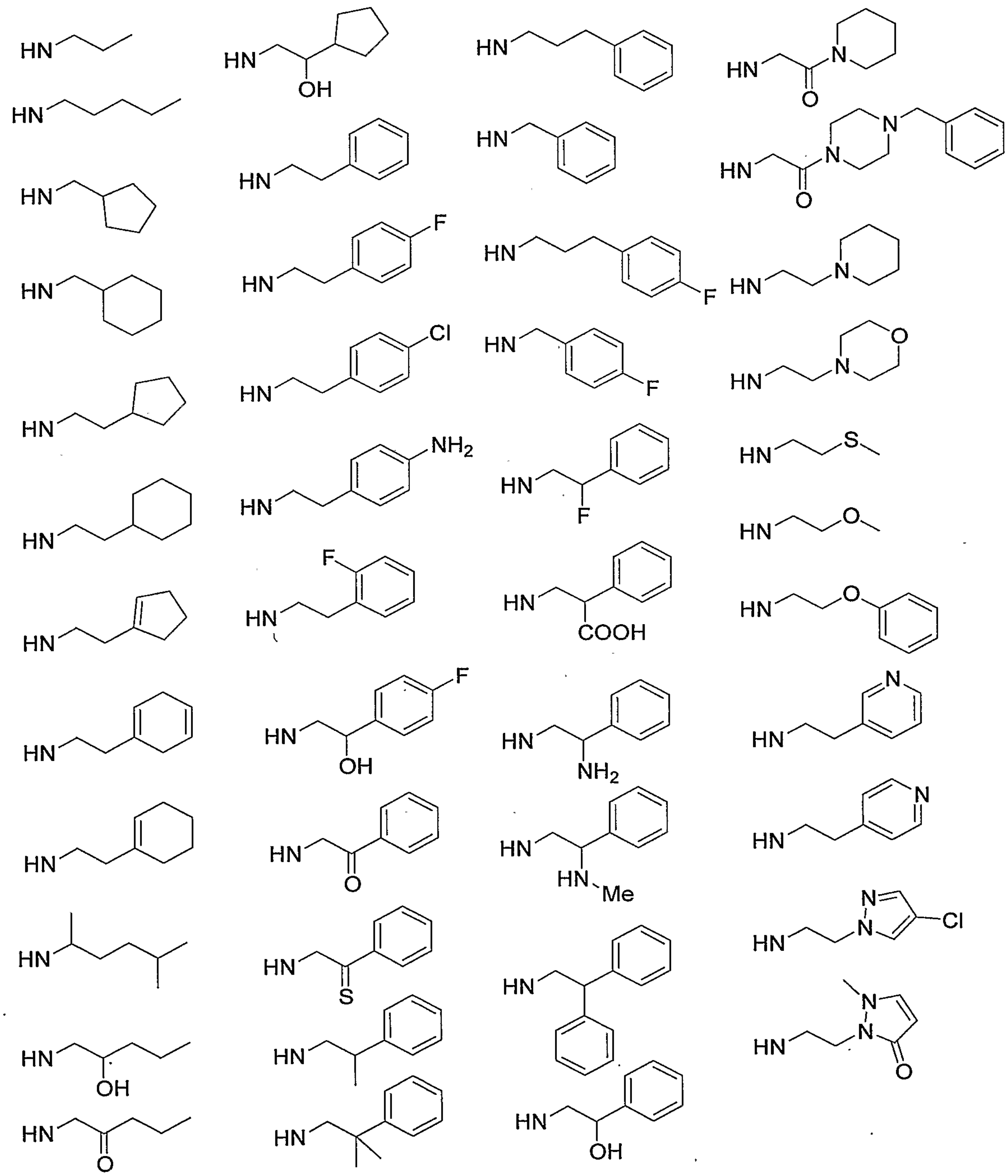

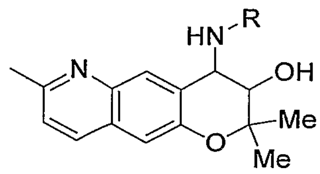

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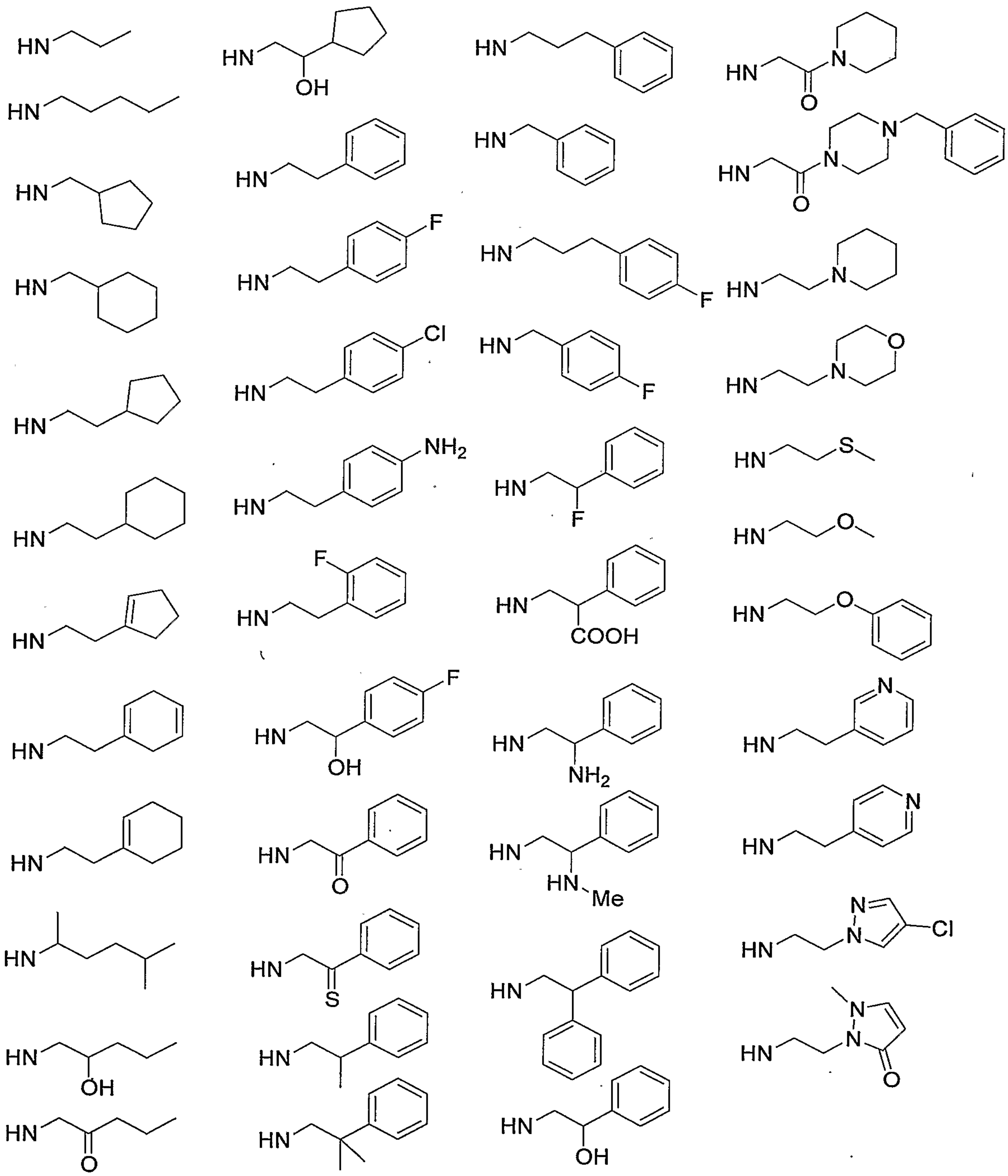

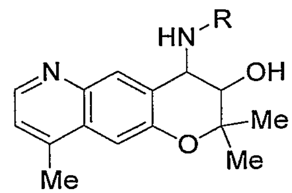

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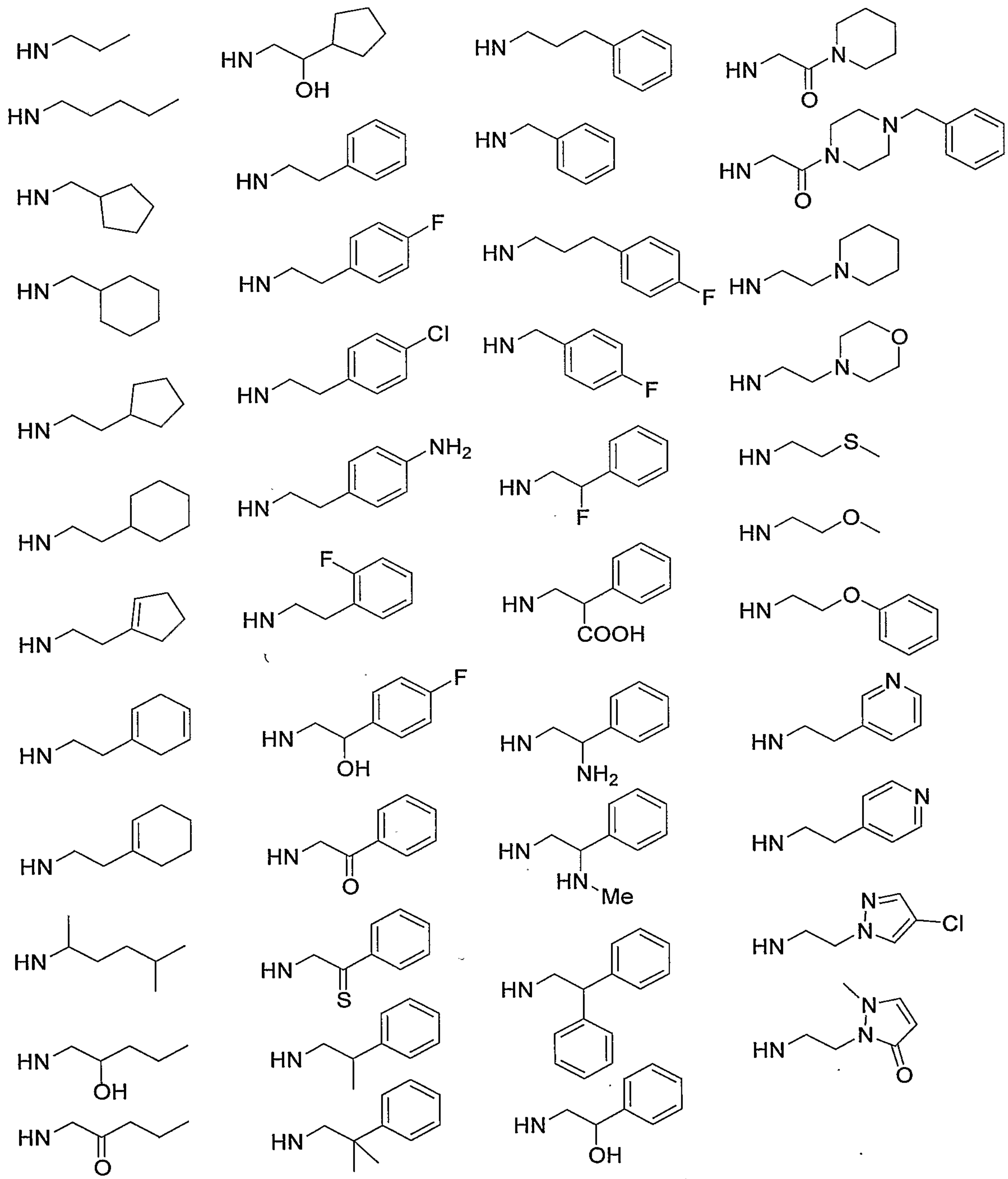

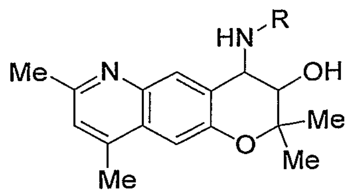

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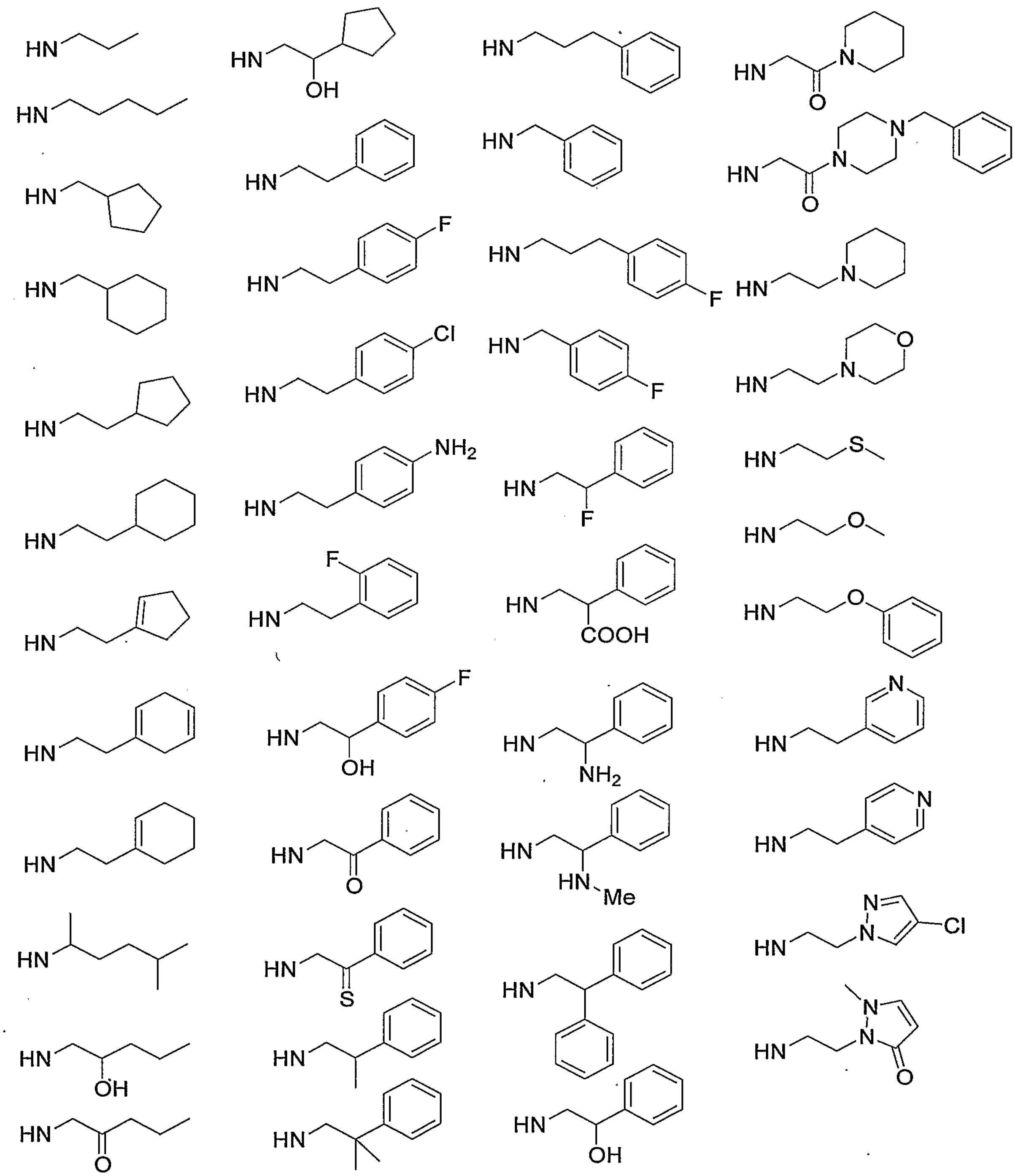

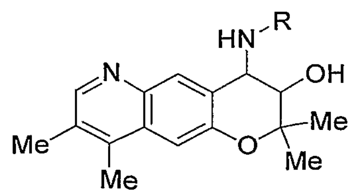

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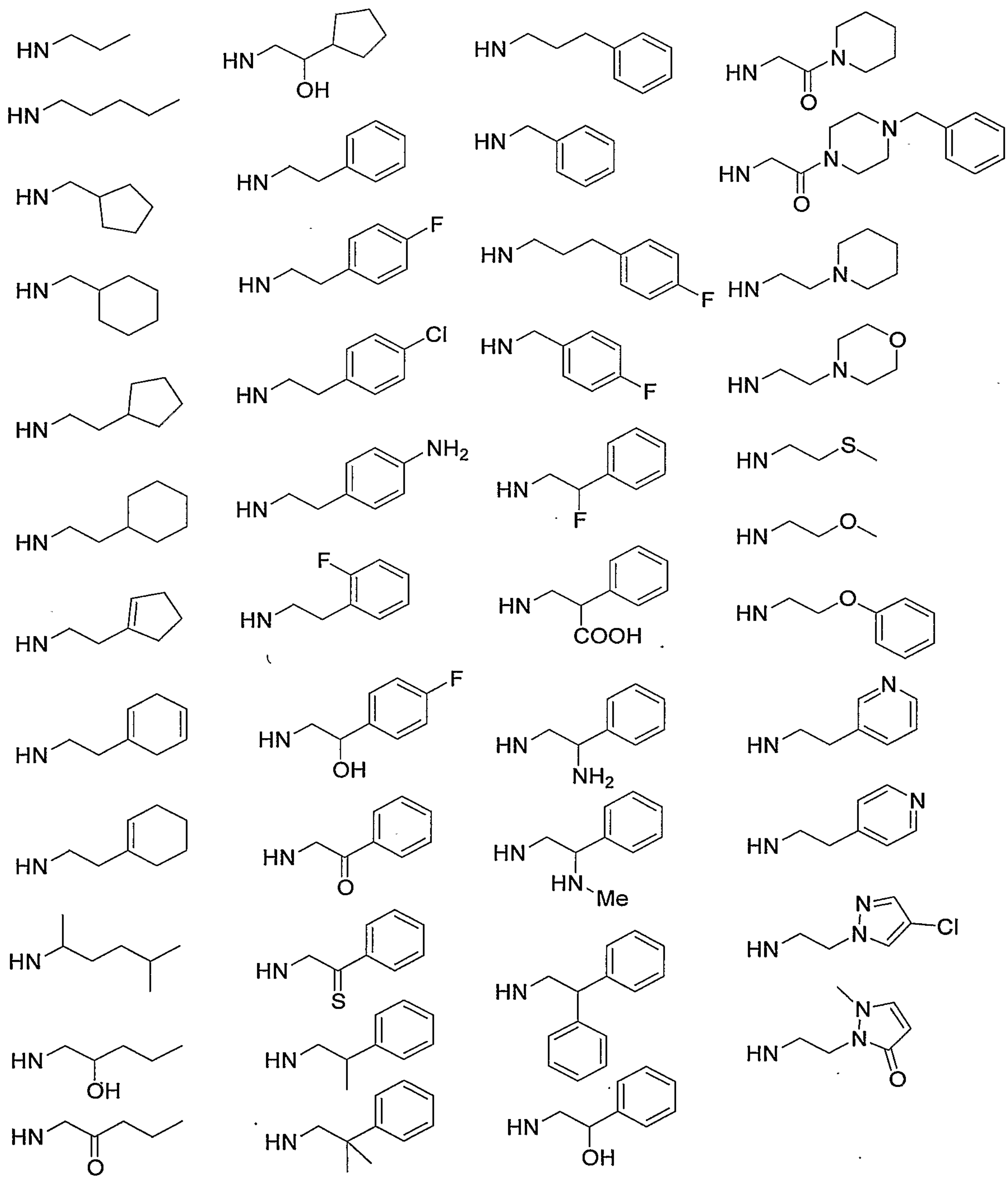

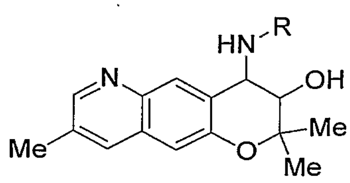

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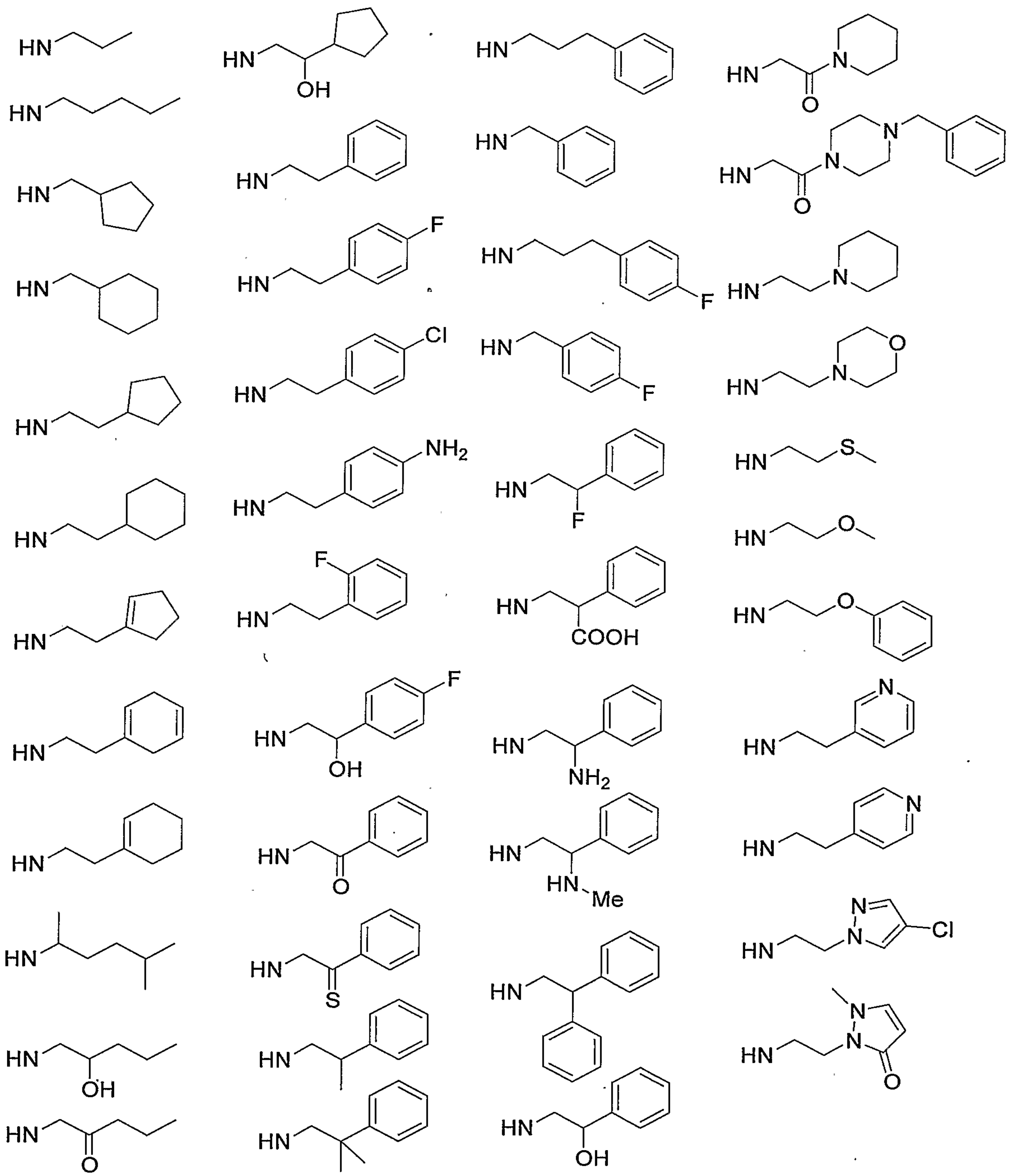

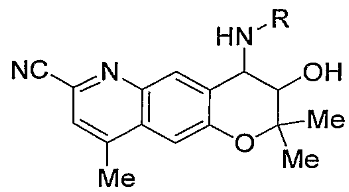

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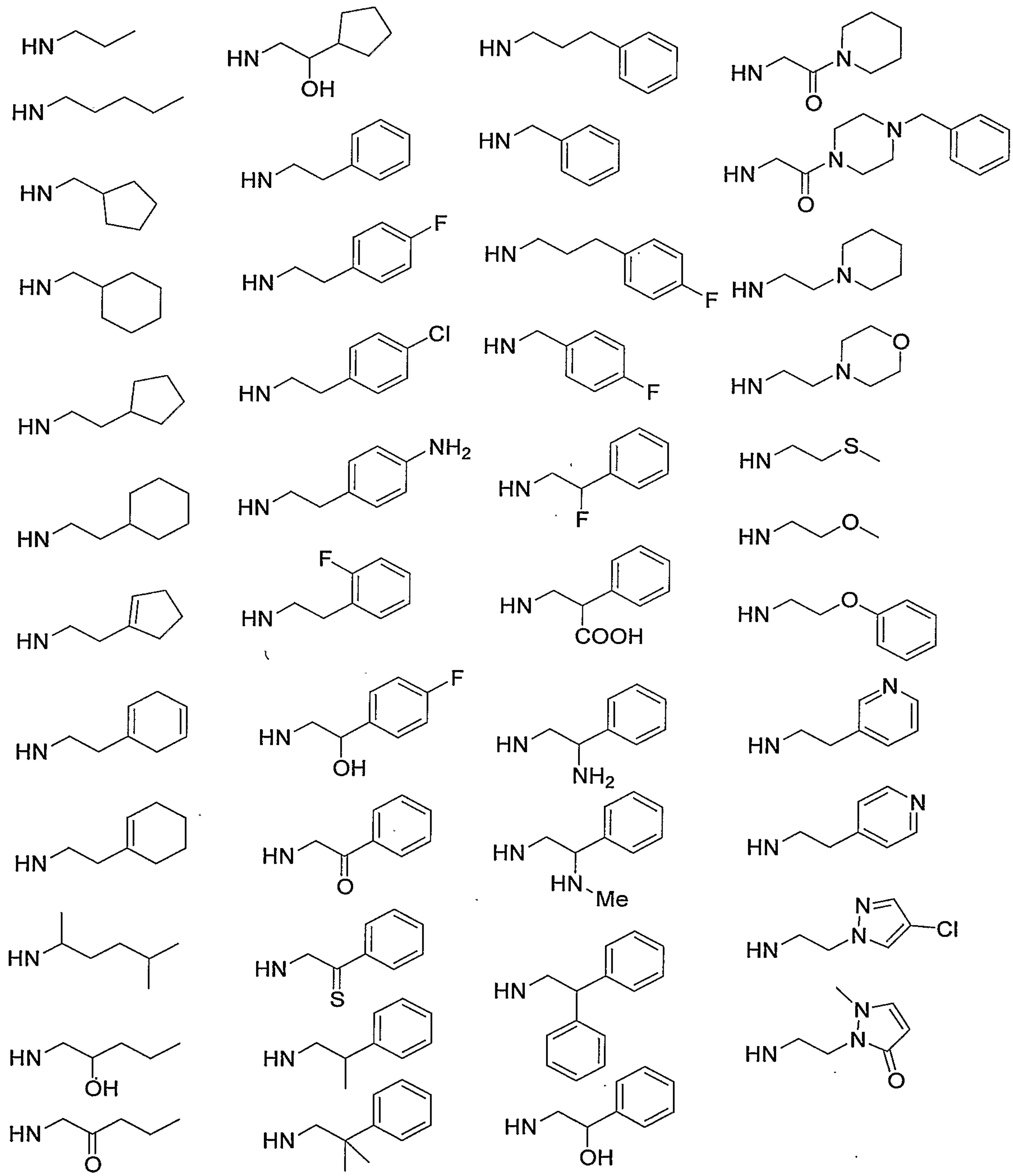

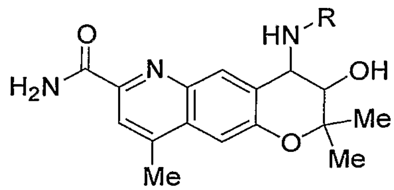

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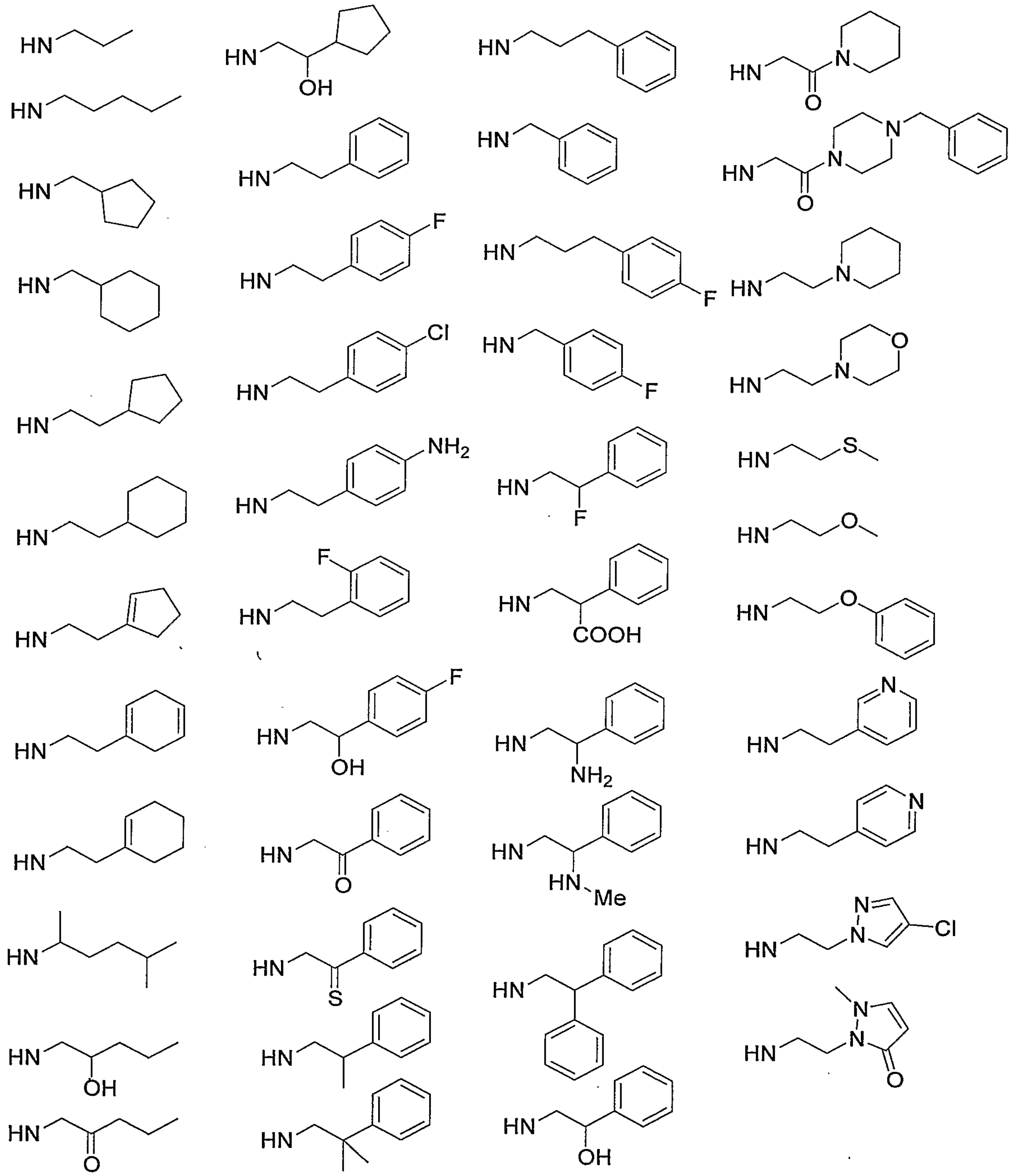

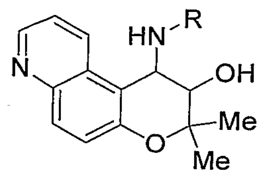

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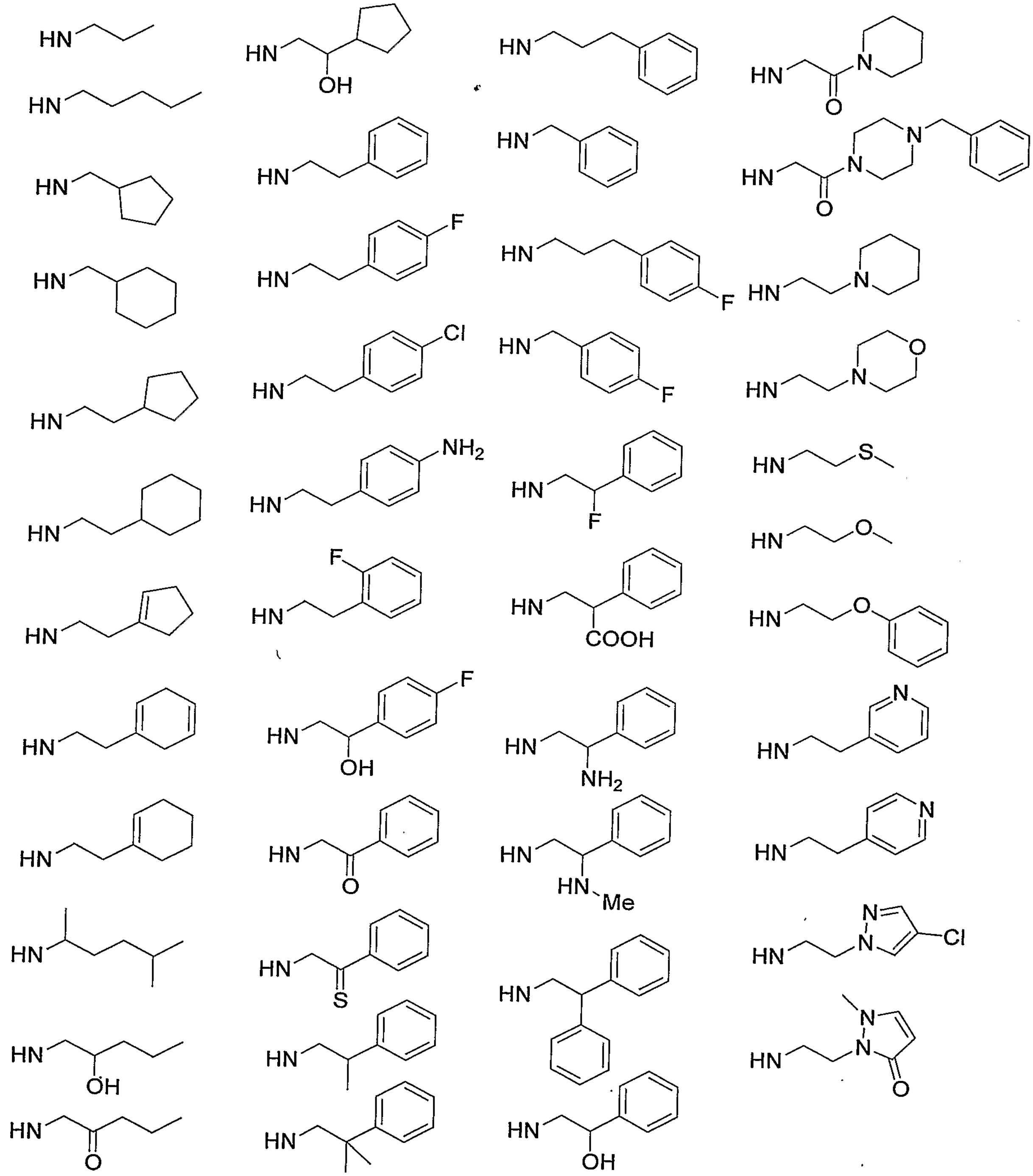

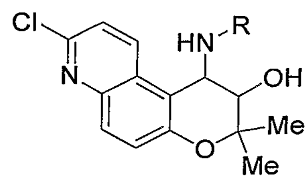

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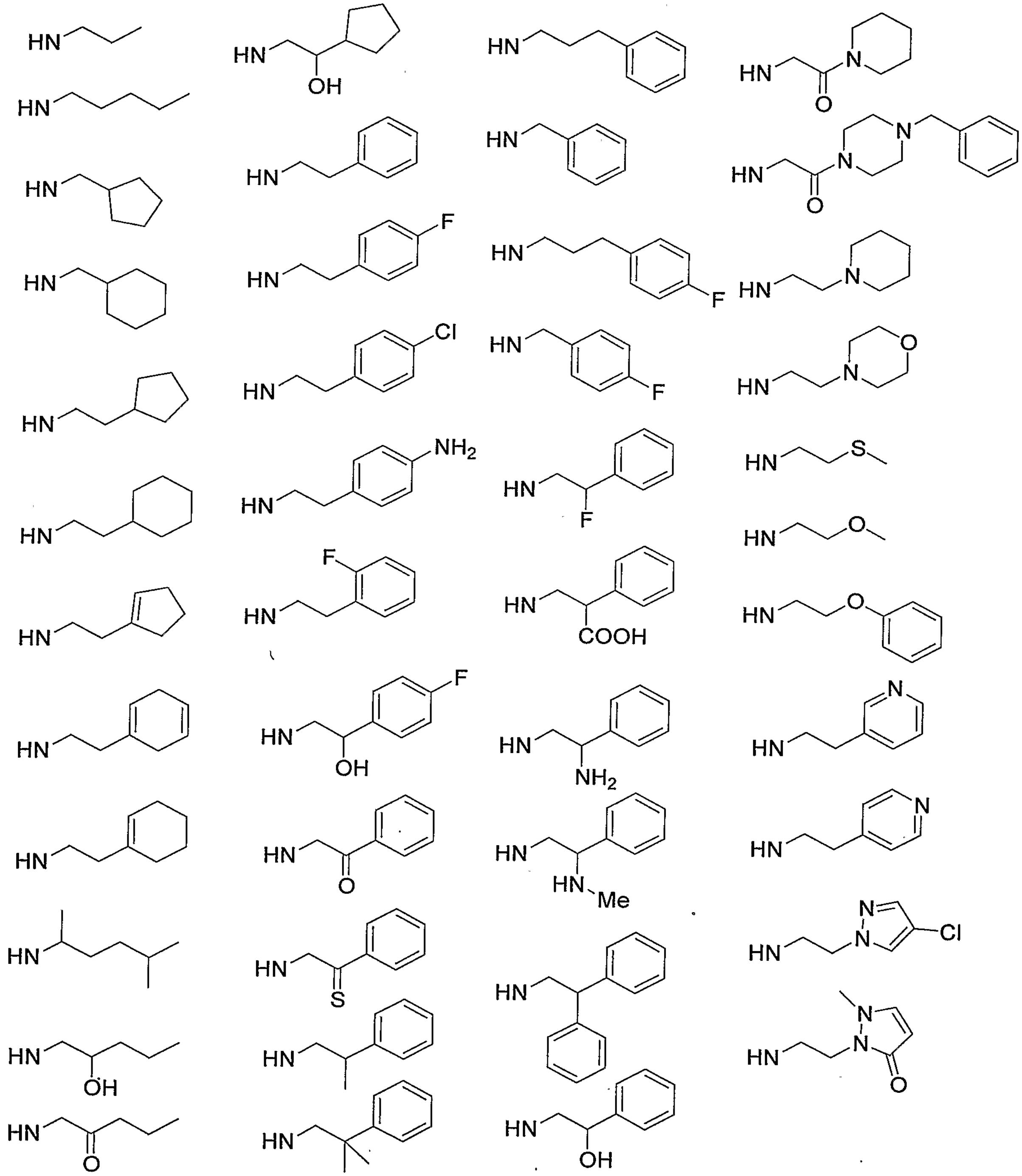

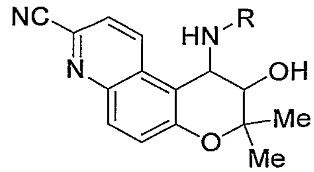

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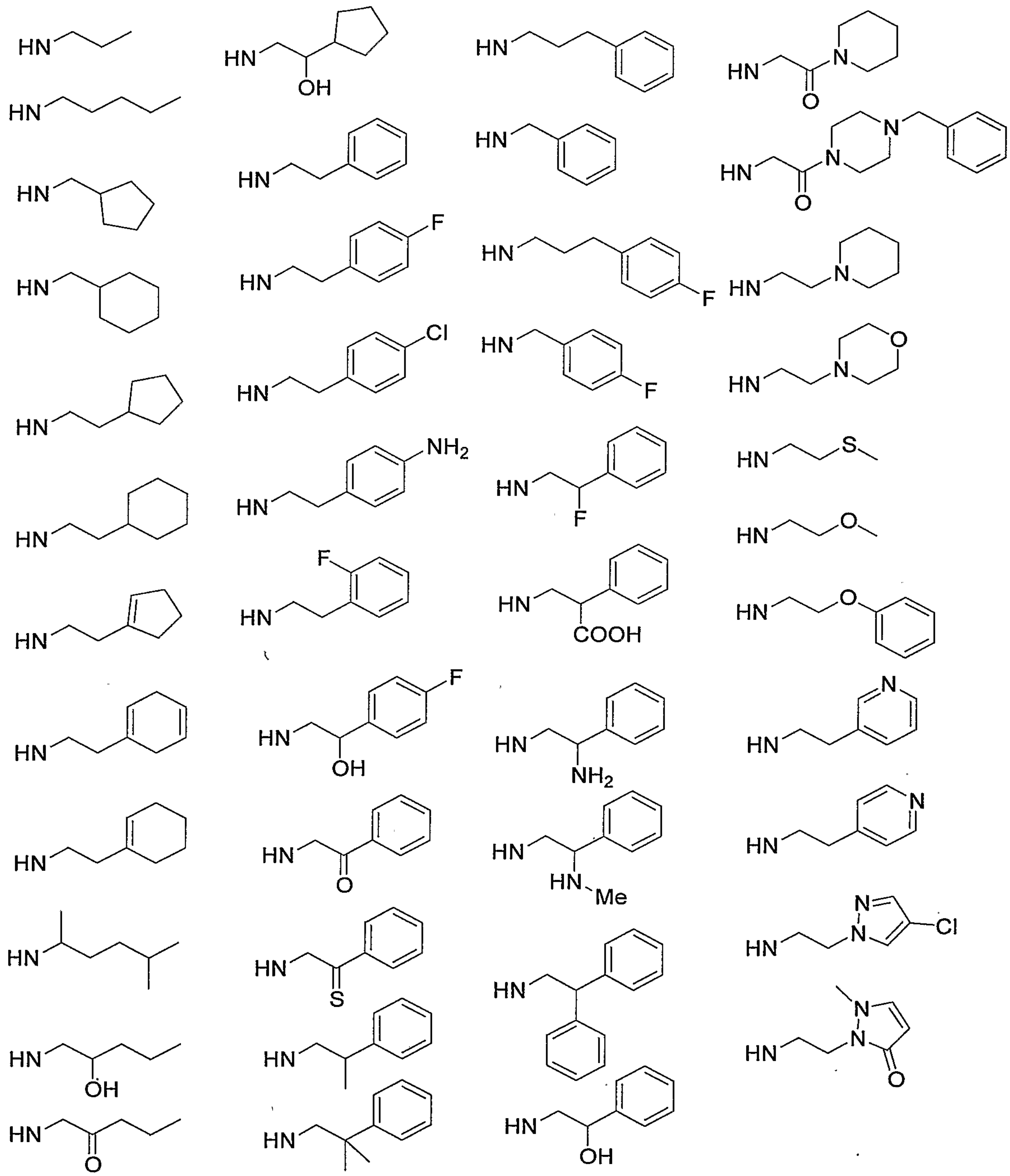

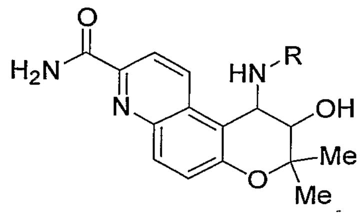

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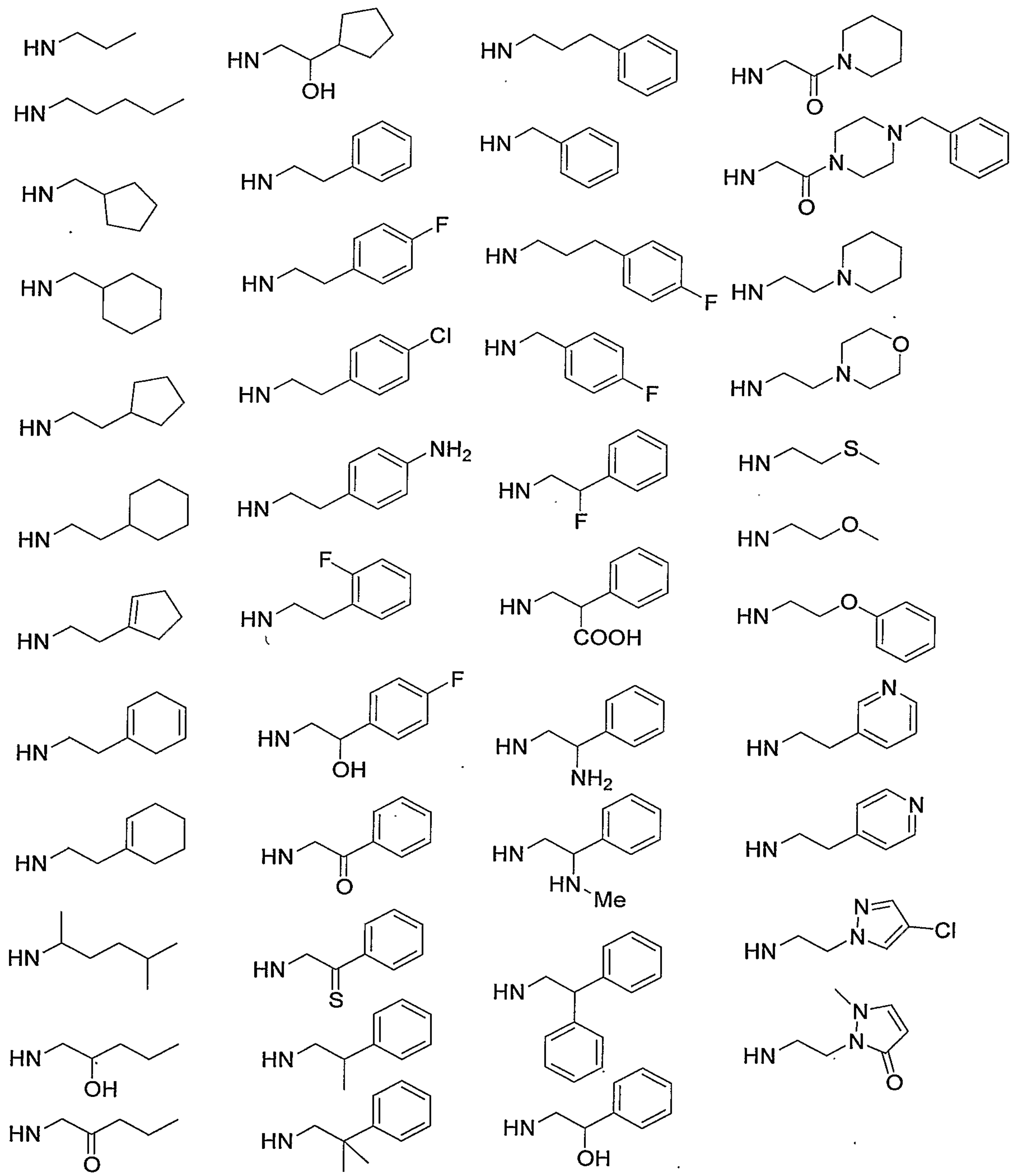

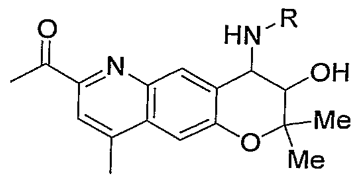

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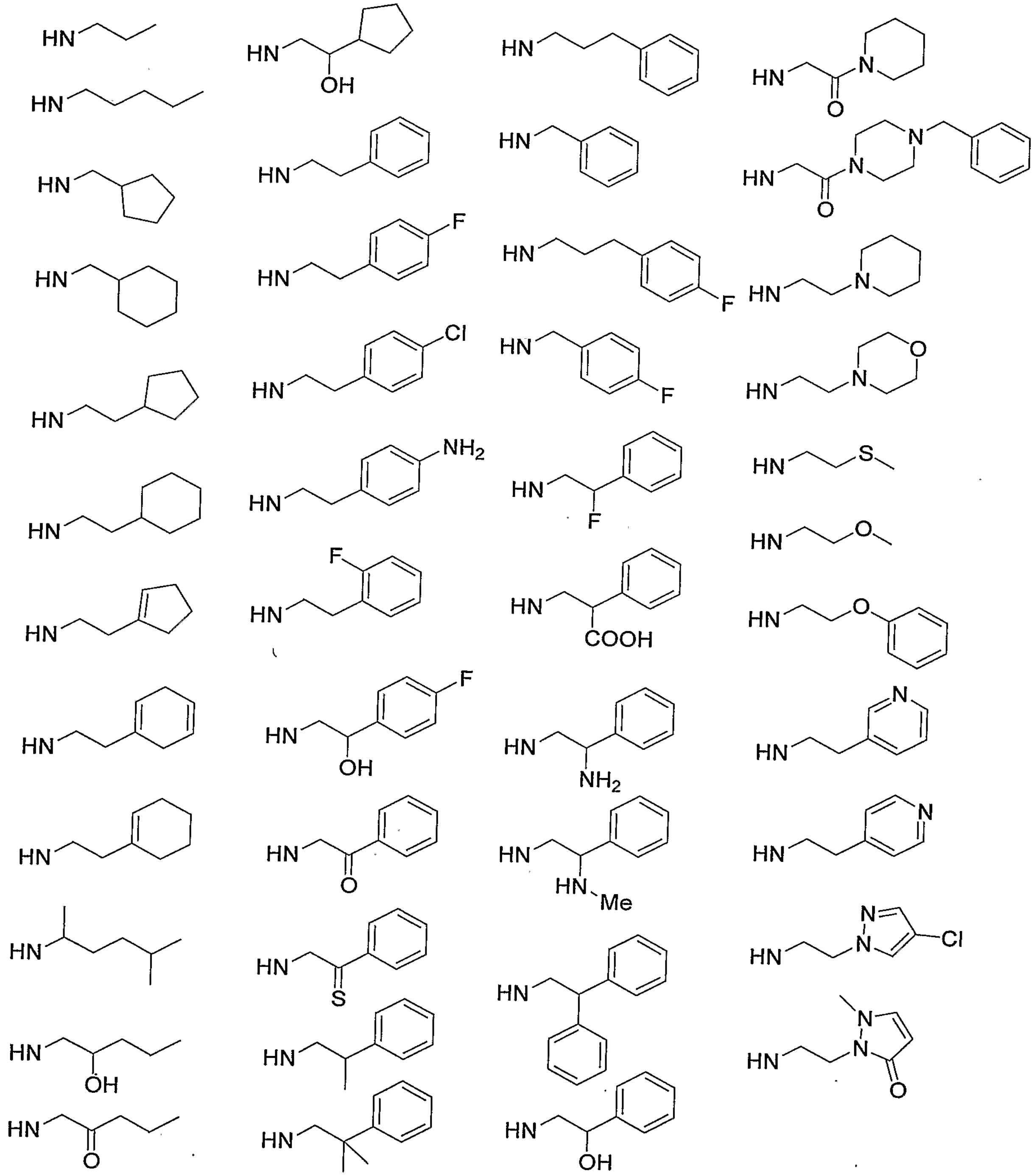

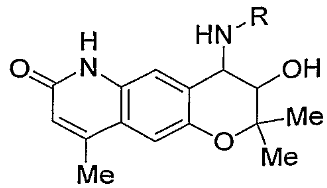

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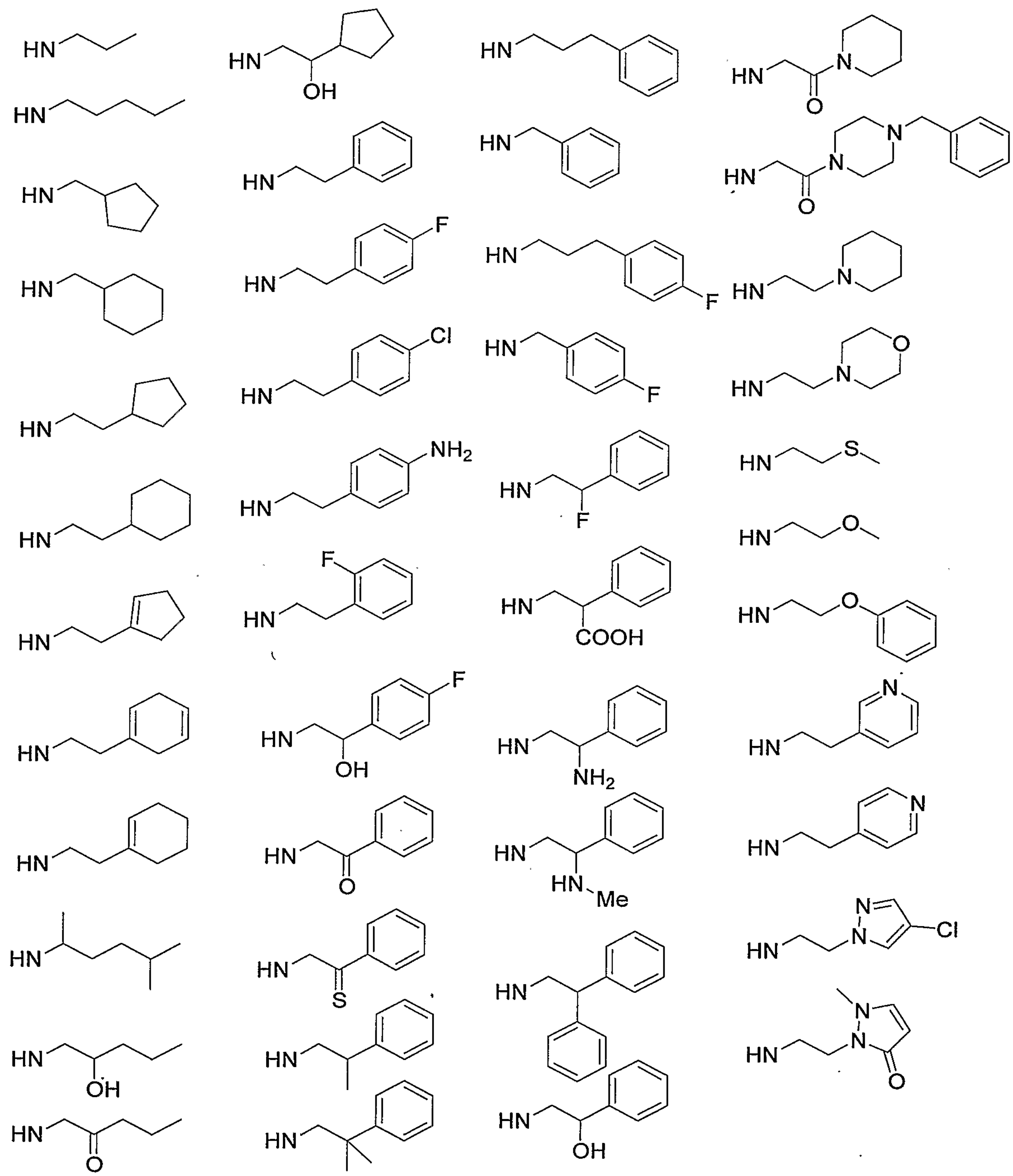

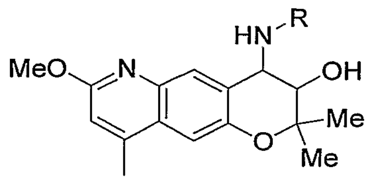

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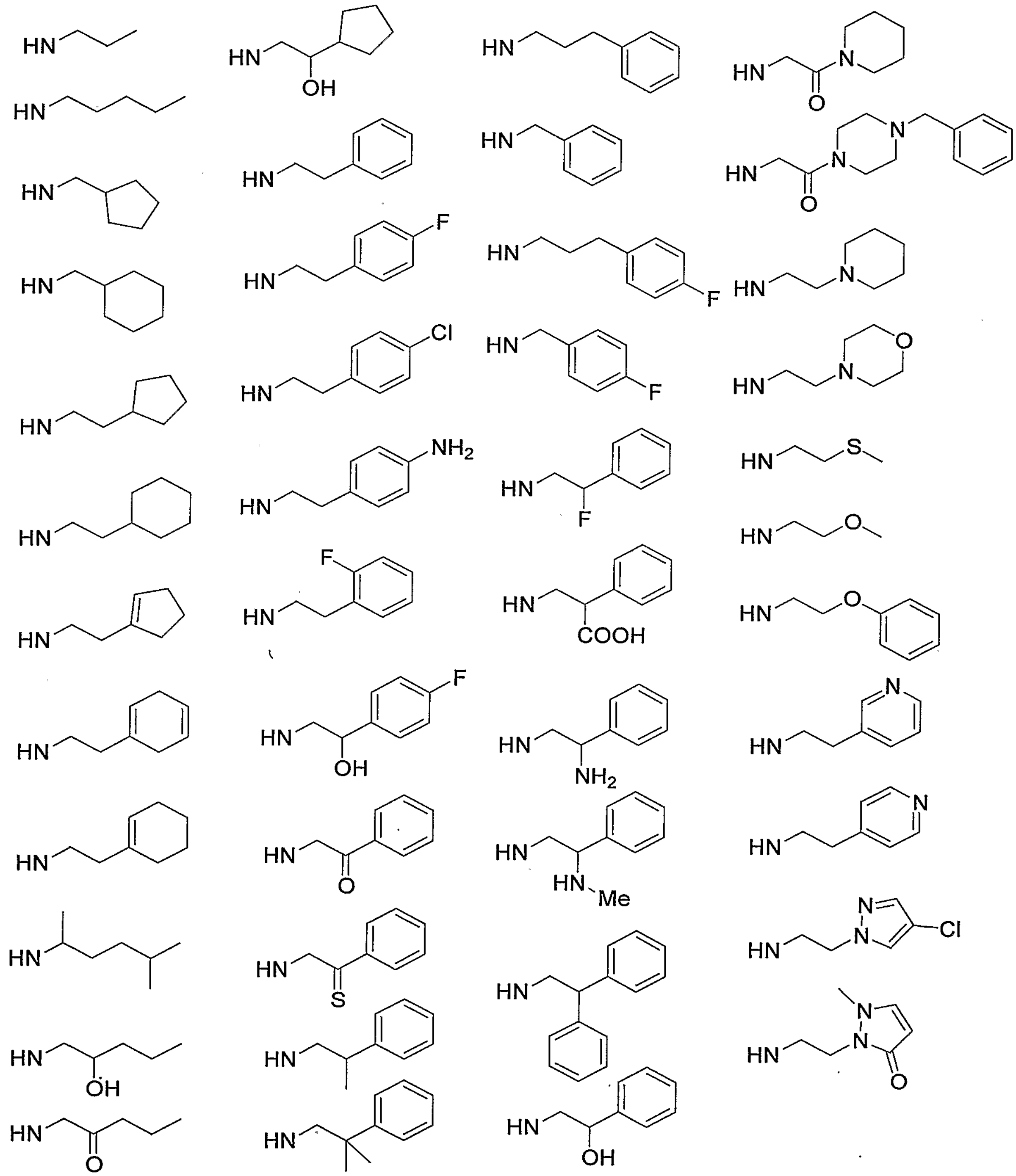

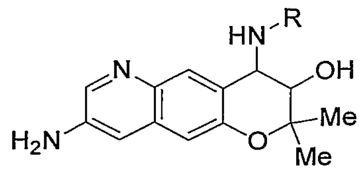

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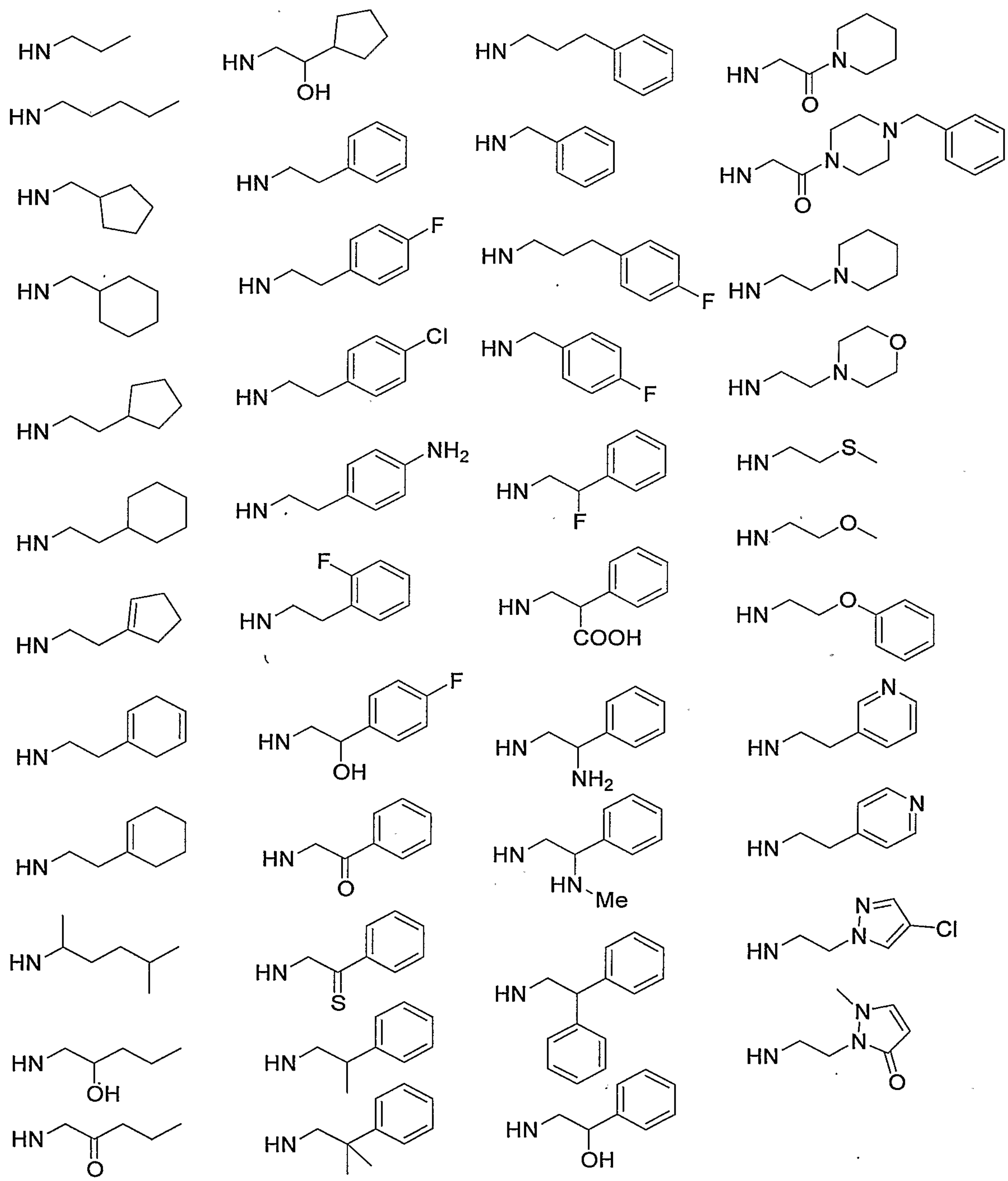

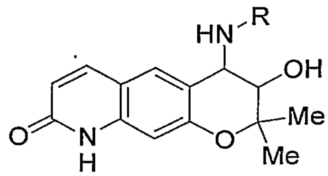

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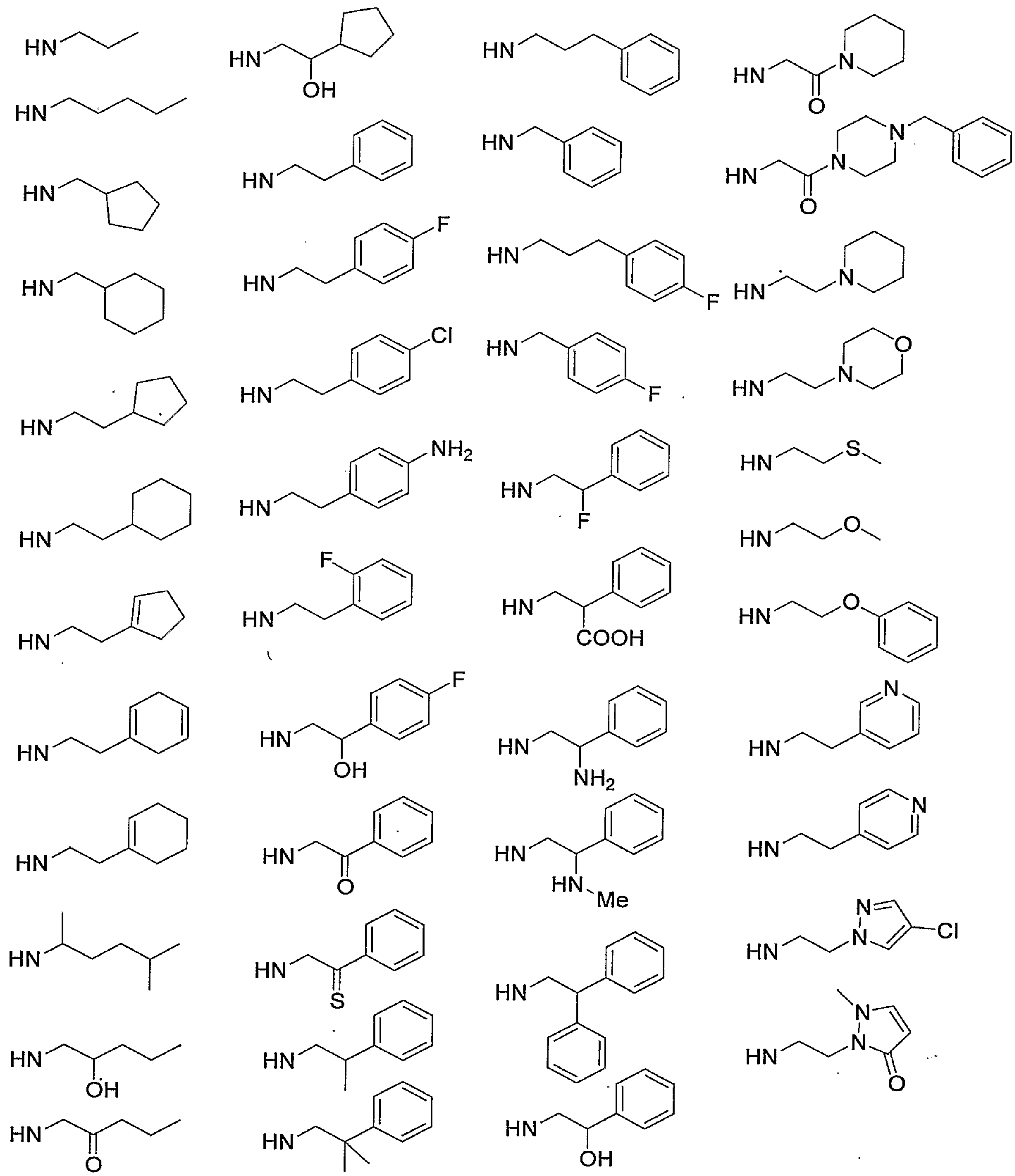

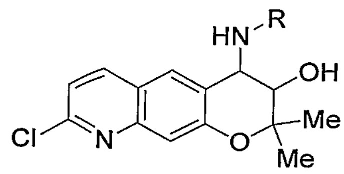

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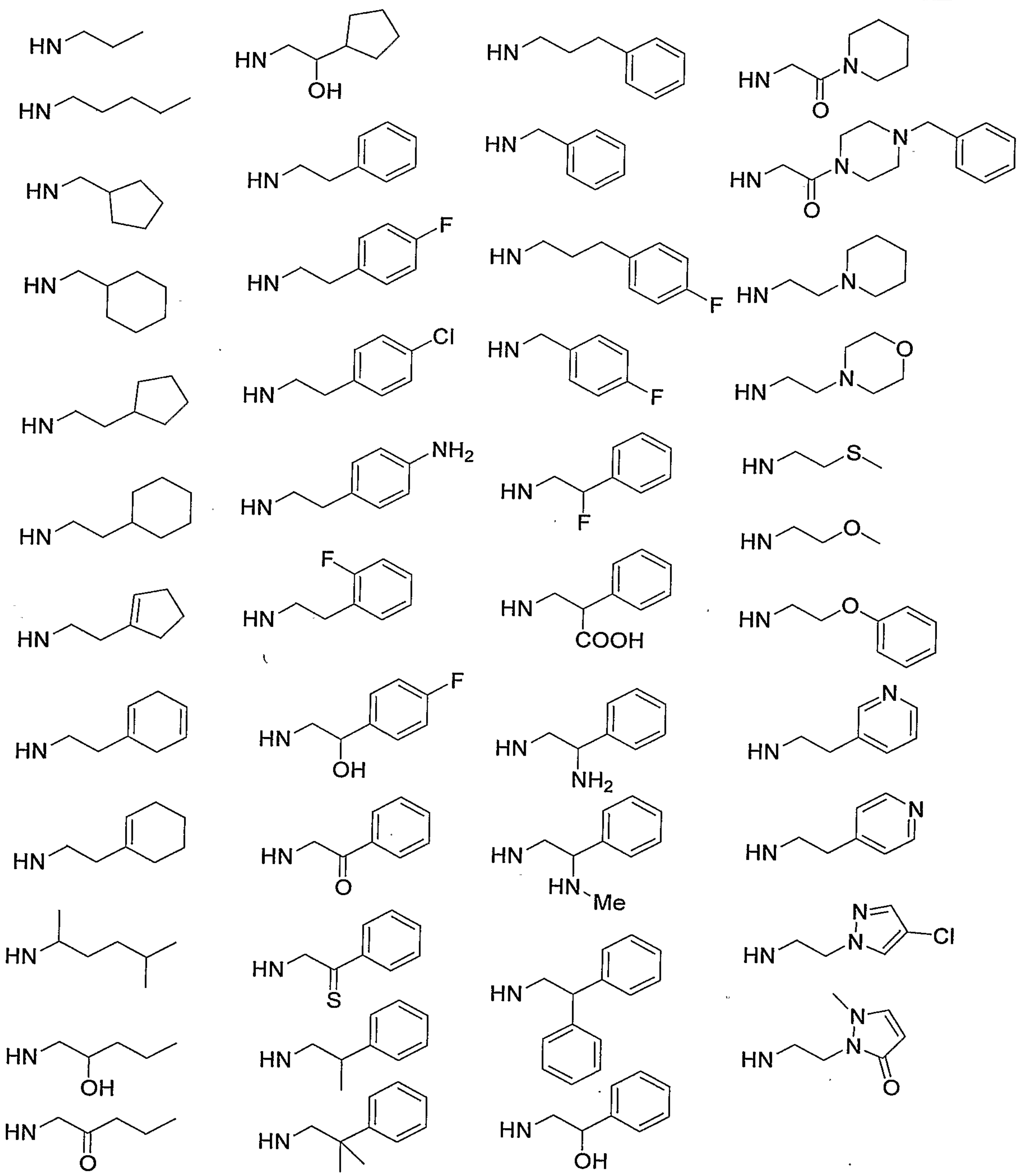

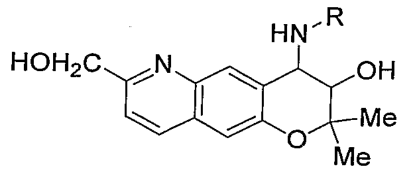

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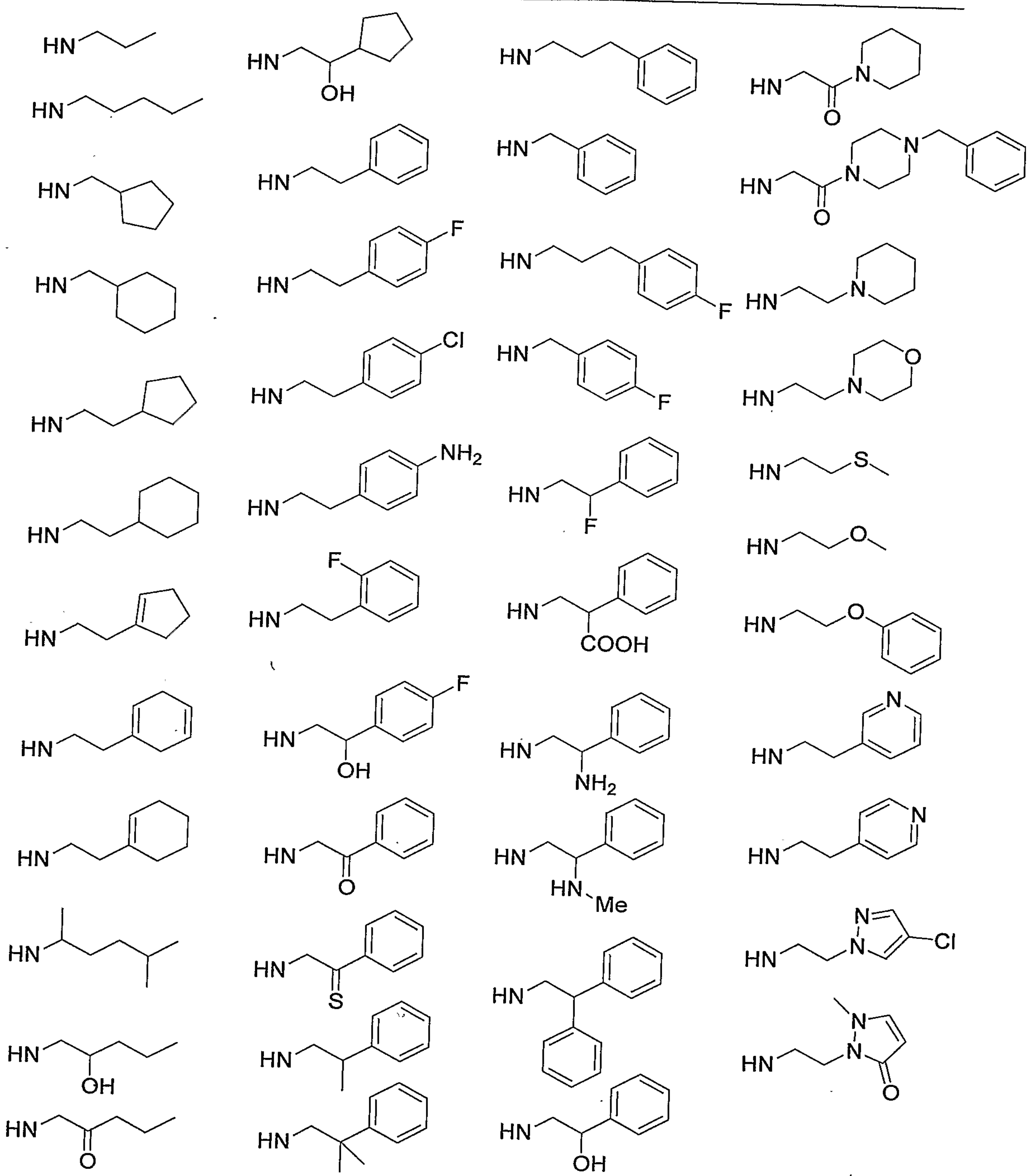

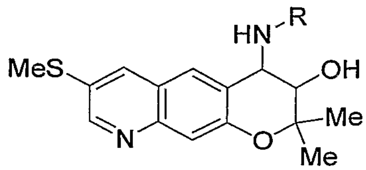

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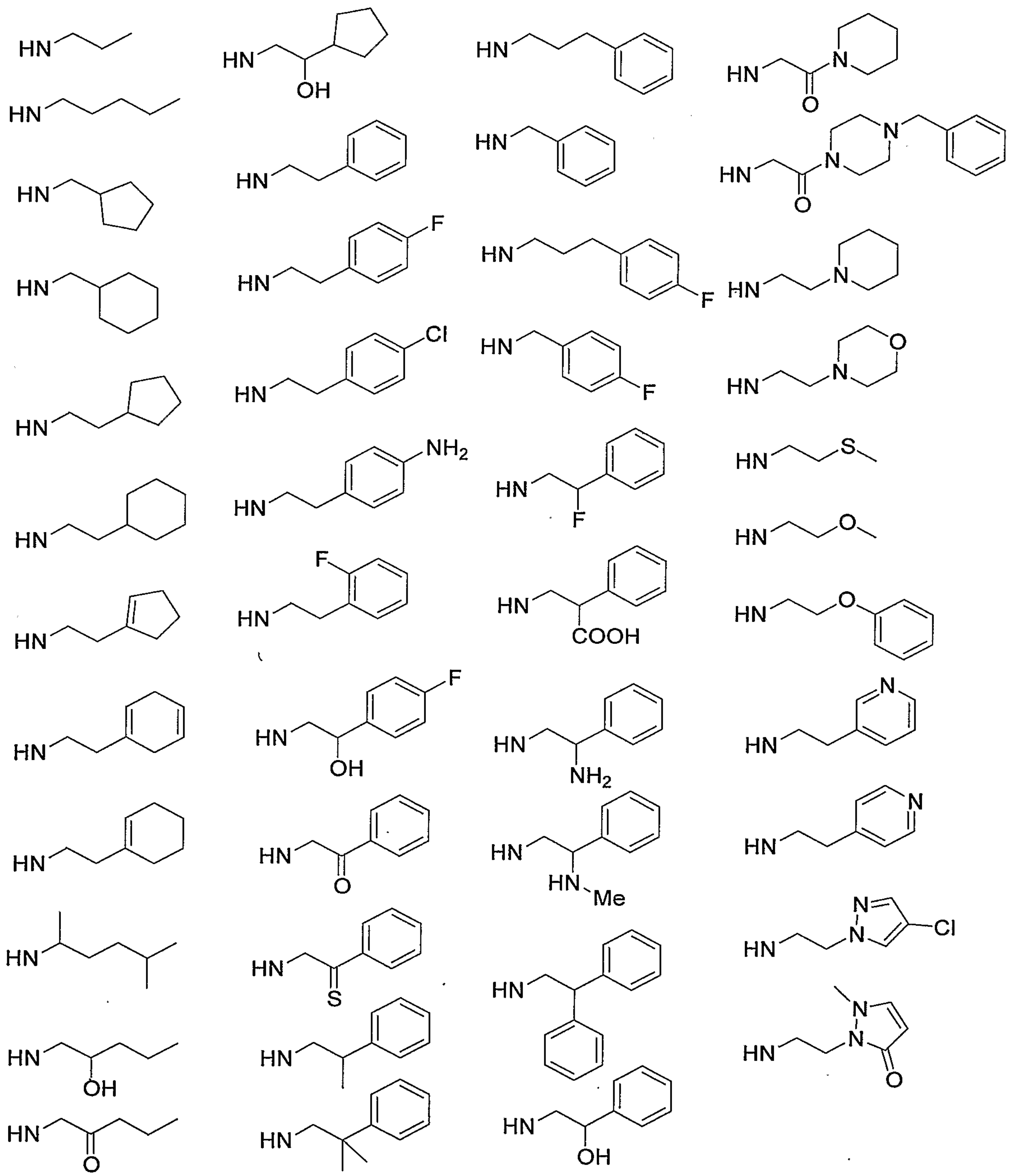

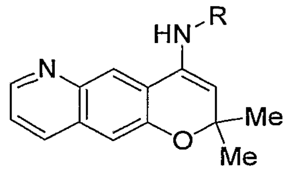

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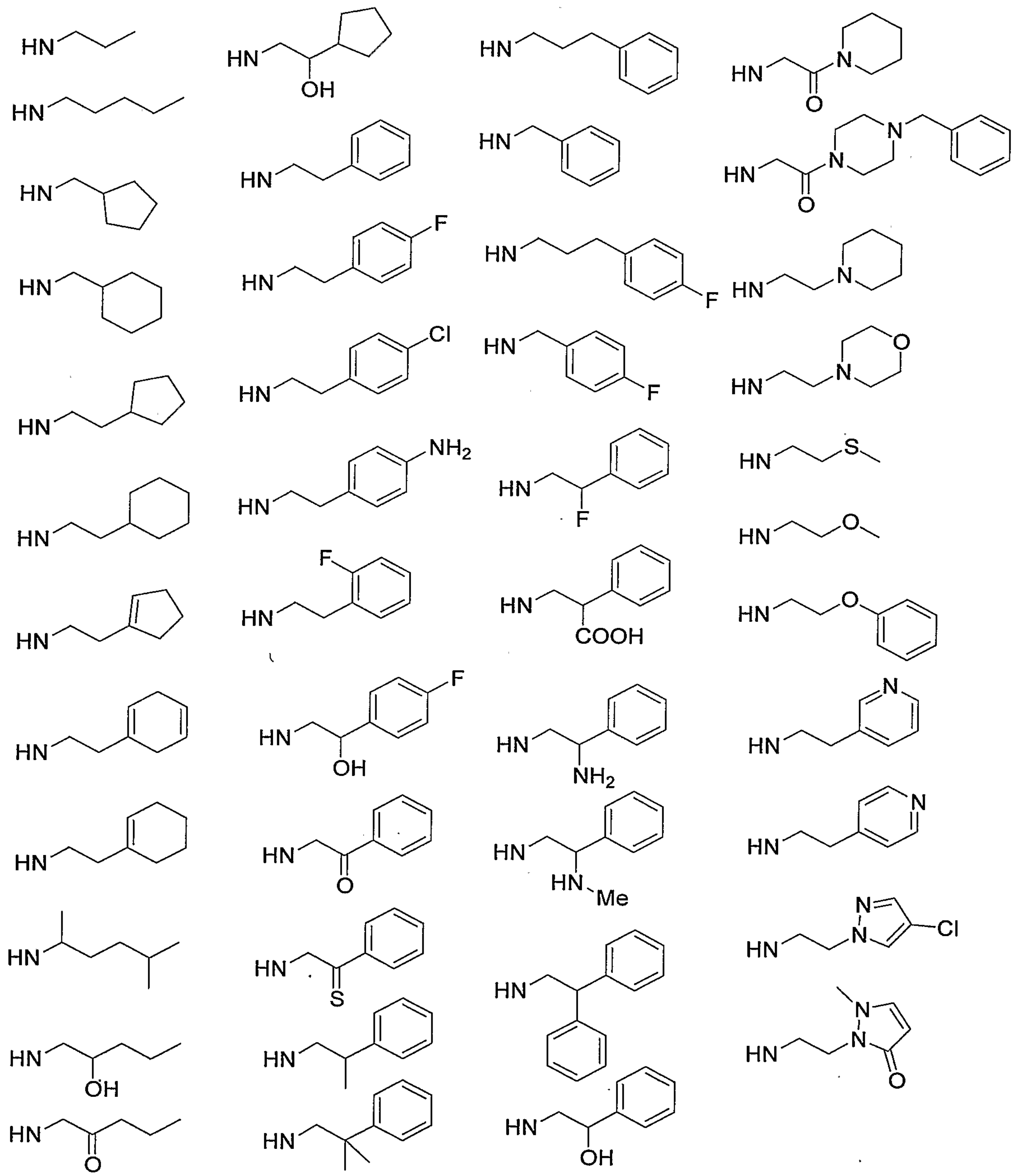

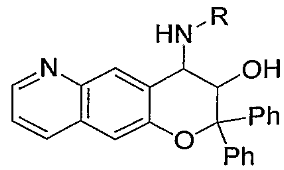

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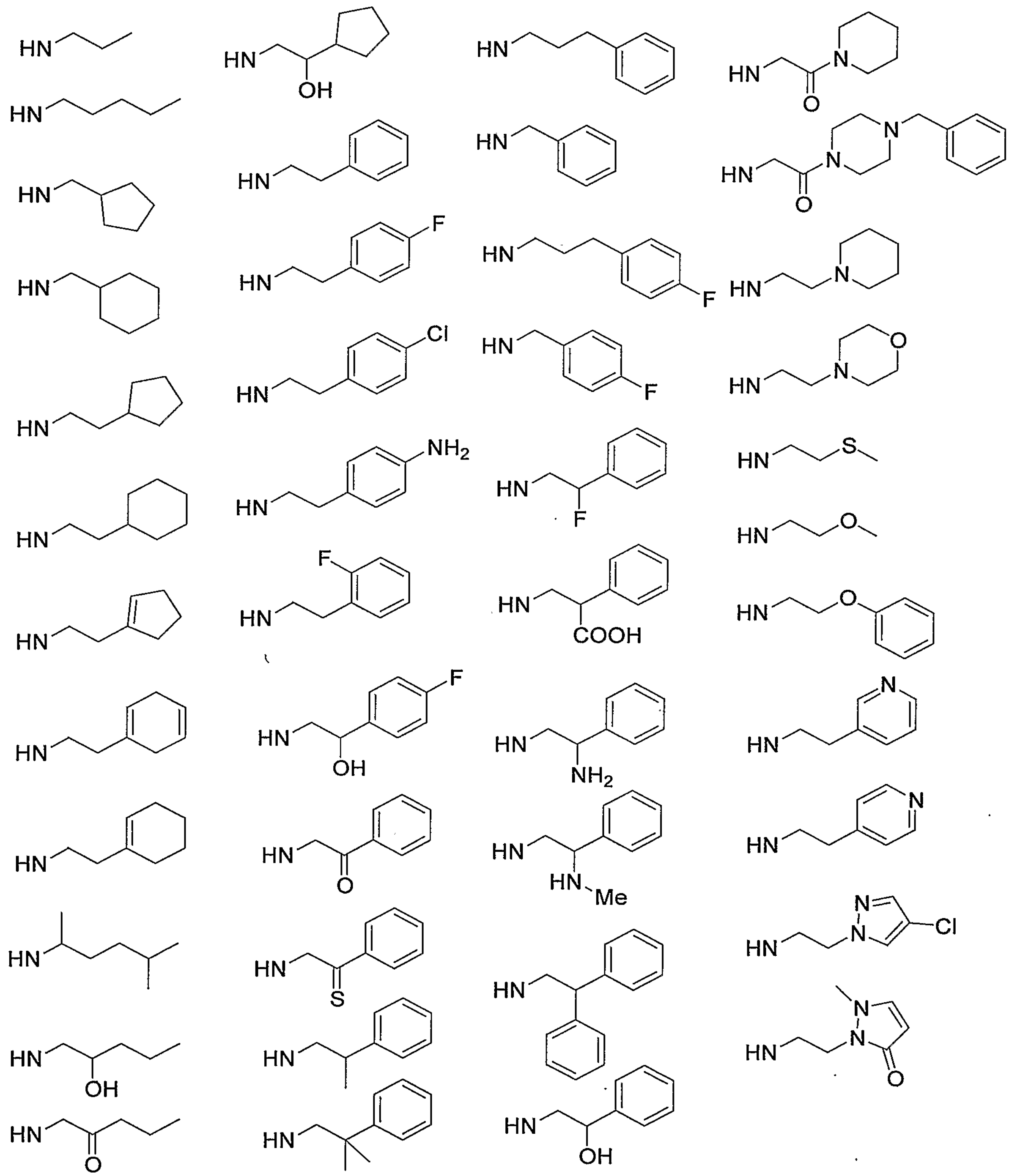

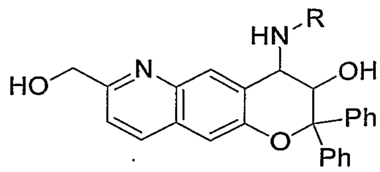

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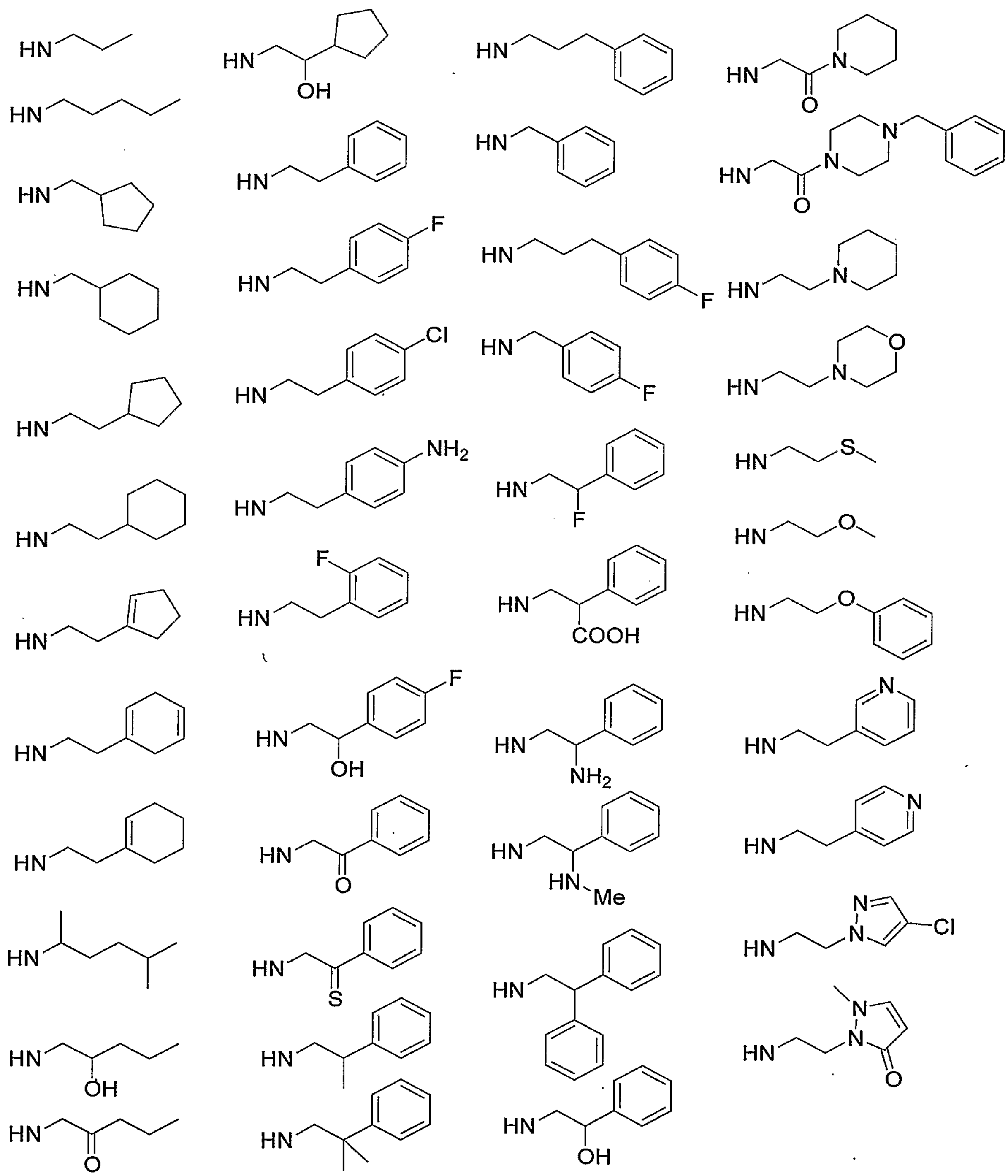

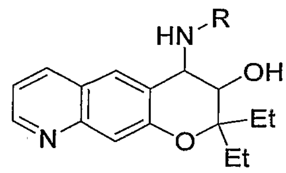

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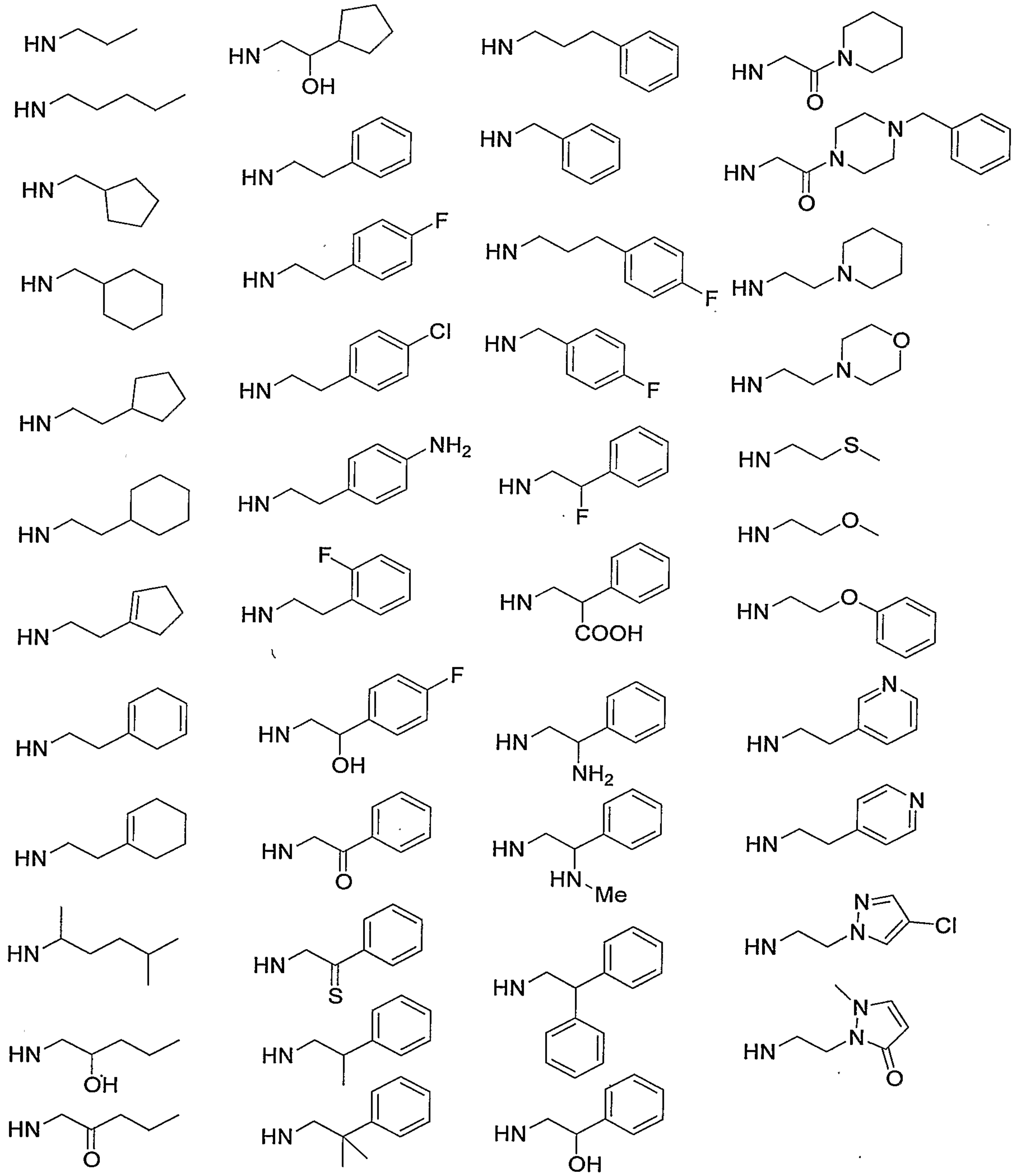

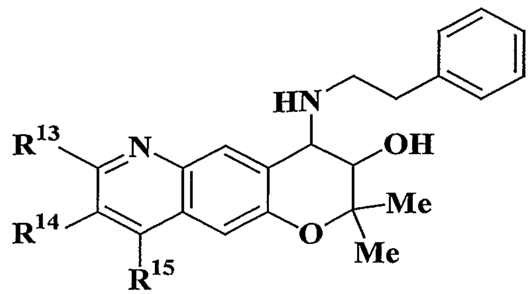

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H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
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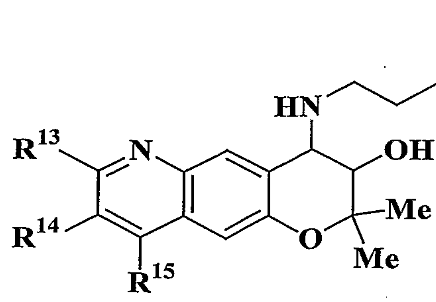

R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
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H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
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Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
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H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
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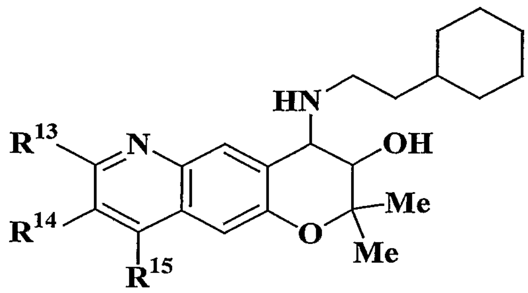

R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
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H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
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Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
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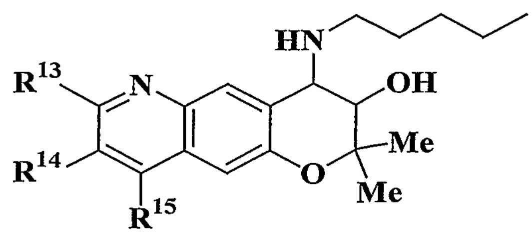

R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
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H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
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Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
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Et	Et	H	OH	Et	H	Et	H	COMe
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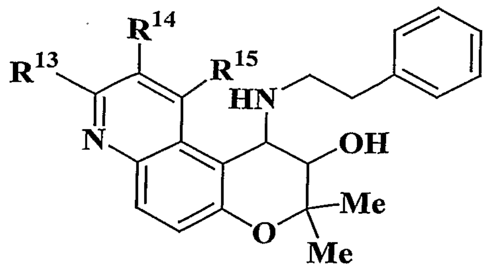

R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
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H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
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Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
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nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
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Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
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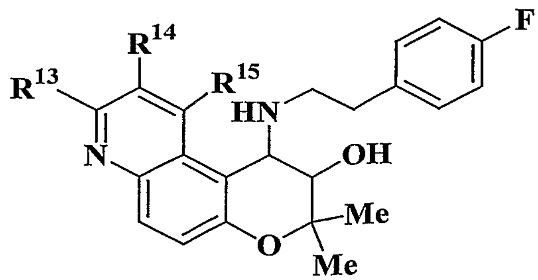
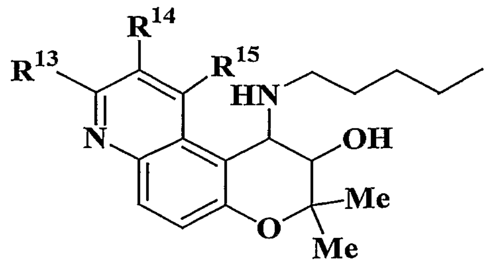
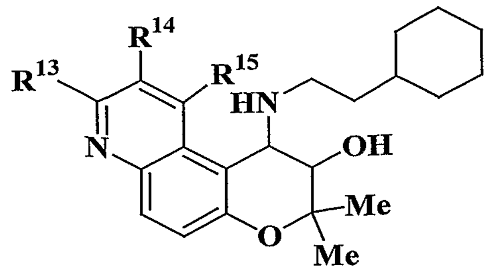


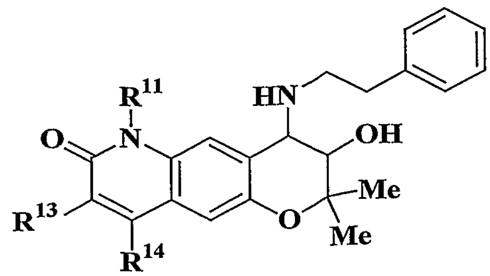
R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



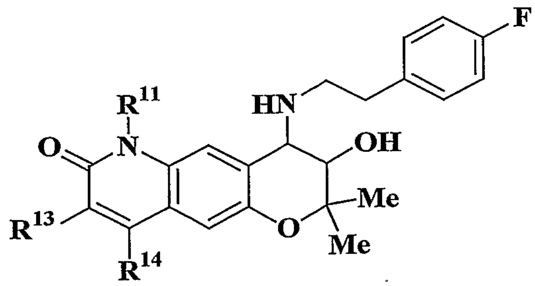
R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}	R^{13}	R^{14}	R^{15}
H	H	Et	NO_2	H	Et	H	NO_2	Et
H	H	iPr	CHO	H	iPr	H	CHO	iPr
H	H	nPr	SO_3H	H	nPr	H	SO_3H	nPr
H	H	nBu	Cl	H	nBu	H	Cl	nBu
H	H	tBu	Br	H	tBu	H	Br	tBu
H	H	Ph	CH_2OH	H	Ph	H	CH_2OH	Ph
Et	H	H	CH_2NH_2	H	H	H	CH_2NH_2	H
iPr	H	H	CH_2NHMe	H	H	H	CH_2NHMe	H
nPr	H	H	CH_2Ph	H	H	H	CH_2Ph	H
nBu	H	H	COMe	H	H	H	COMe	H
tBu	H	H	COOH	H	H	H	COOH	H
Ph	H	H	$CONH_2$	H	H	H	$CONH_2$	H
H	Et	H	CONHMe	Et	H	Et	CONHMe	H
H	iPr	H	CONHMs	iPr	H	iPr	CONHMs	H
H	nPr	H	NHMs	nPr	H	nPr	NHMs	H
H	nBu	H	NHCOMe	nBu	H	nBu	NHCOMe	H
H	tBu	H	NO_2	tBu	H	tBu	NO_2	H
H	Ph	H	CHO	Ph	H	Ph	H	SO_3H
Cl	Et	H	SO_3H	Et	H	Et	H	SO_2NHMe
Cl	nPr	H	SO_2NHMe	nPr	H	nPr	H	OH
Cl	Ph	H	OH	Ph	H	Ph	H	COMe
Et	Cl	H	COMe	Cl	H	Cl	Cl	COOH
nPr	Cl	H	COOH	Cl	H	Cl	Cl	$CONH_2$
Ph	Cl	H	$CONH_2$	Cl	H	Cl	Cl	CONHMe
H	Et	Cl	CONHMe	Et	Cl	Et	H	CONHMs
H	nPr	Cl	CONHMs	nPr	Cl	nPr	H	NHMs
H	Ph	Cl	NHMs	Ph	Cl	Ph	H	NO_2
Me	Me	H	NO_2	Me	H	Me	H	OH
Et	Et	H	OH	Et	H	Et	H	COMe
nPr	nPr	H	COMe	nPr	H	nPr	H	COOH
Ph	Ph	H	COOH	Ph	H	Ph	H	NO_2



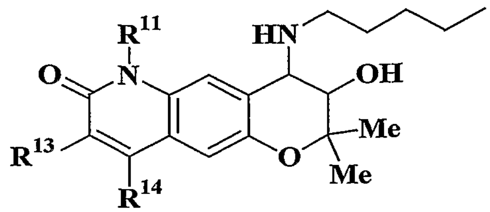
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	H
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

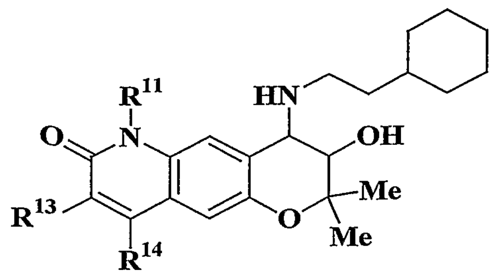
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



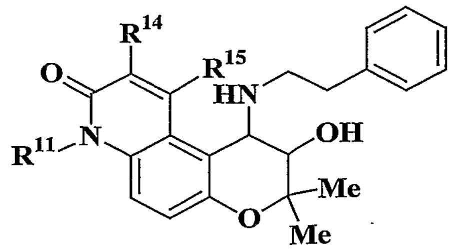
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	H
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



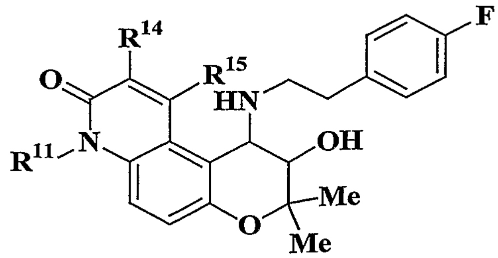
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	H
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

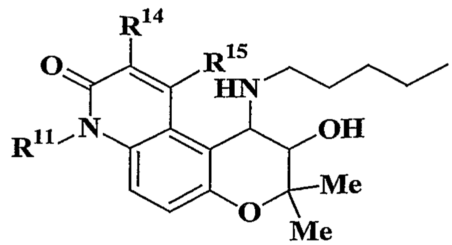
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



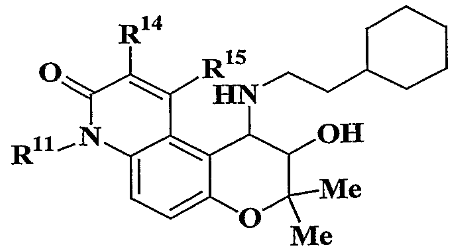
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	H
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

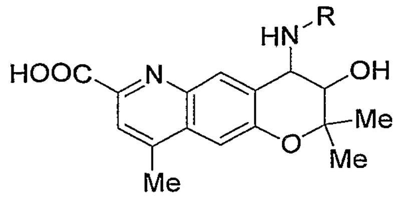
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	H	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



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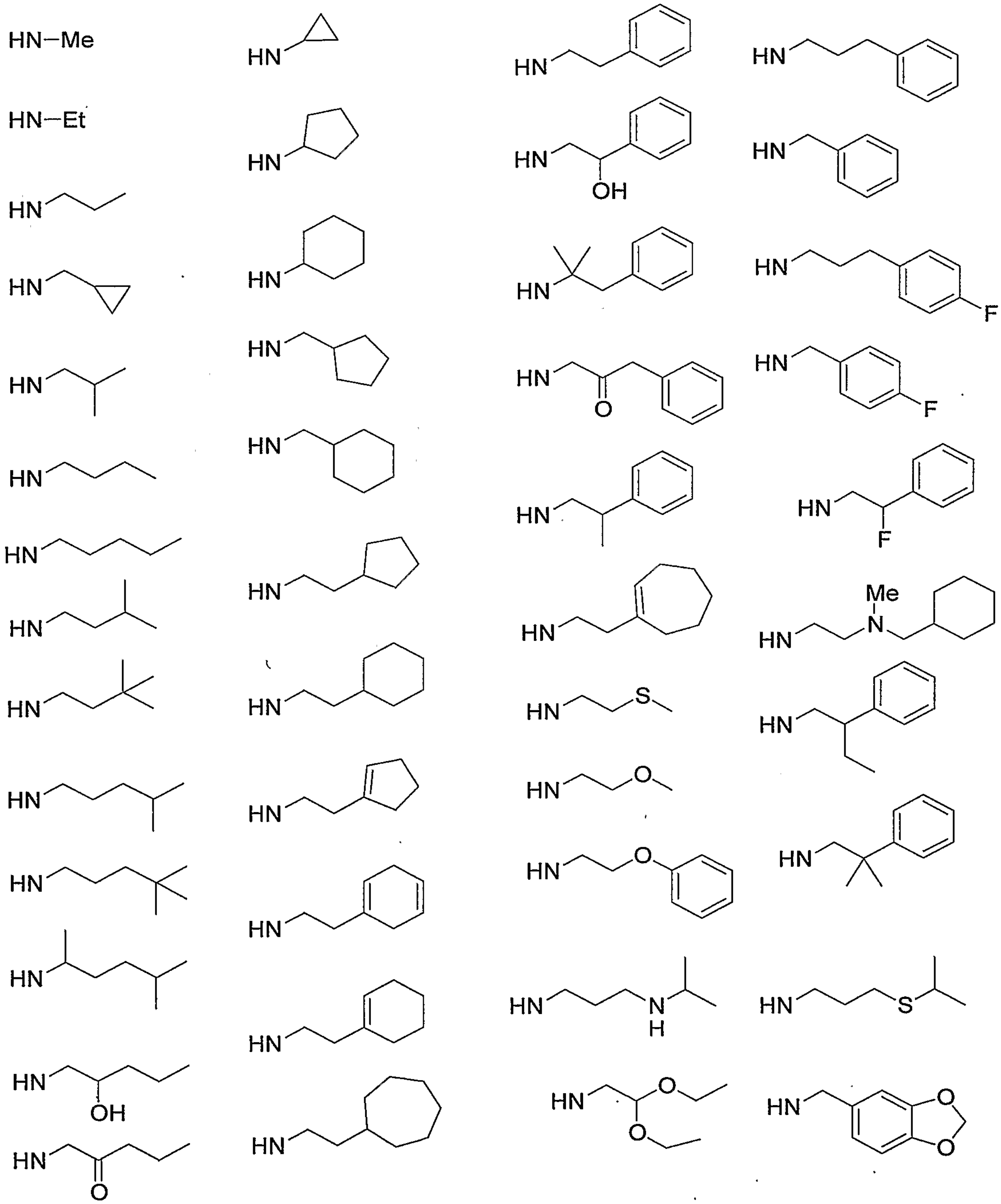

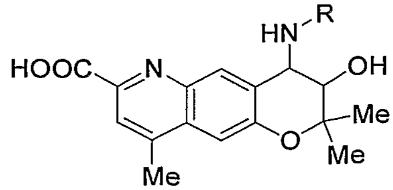

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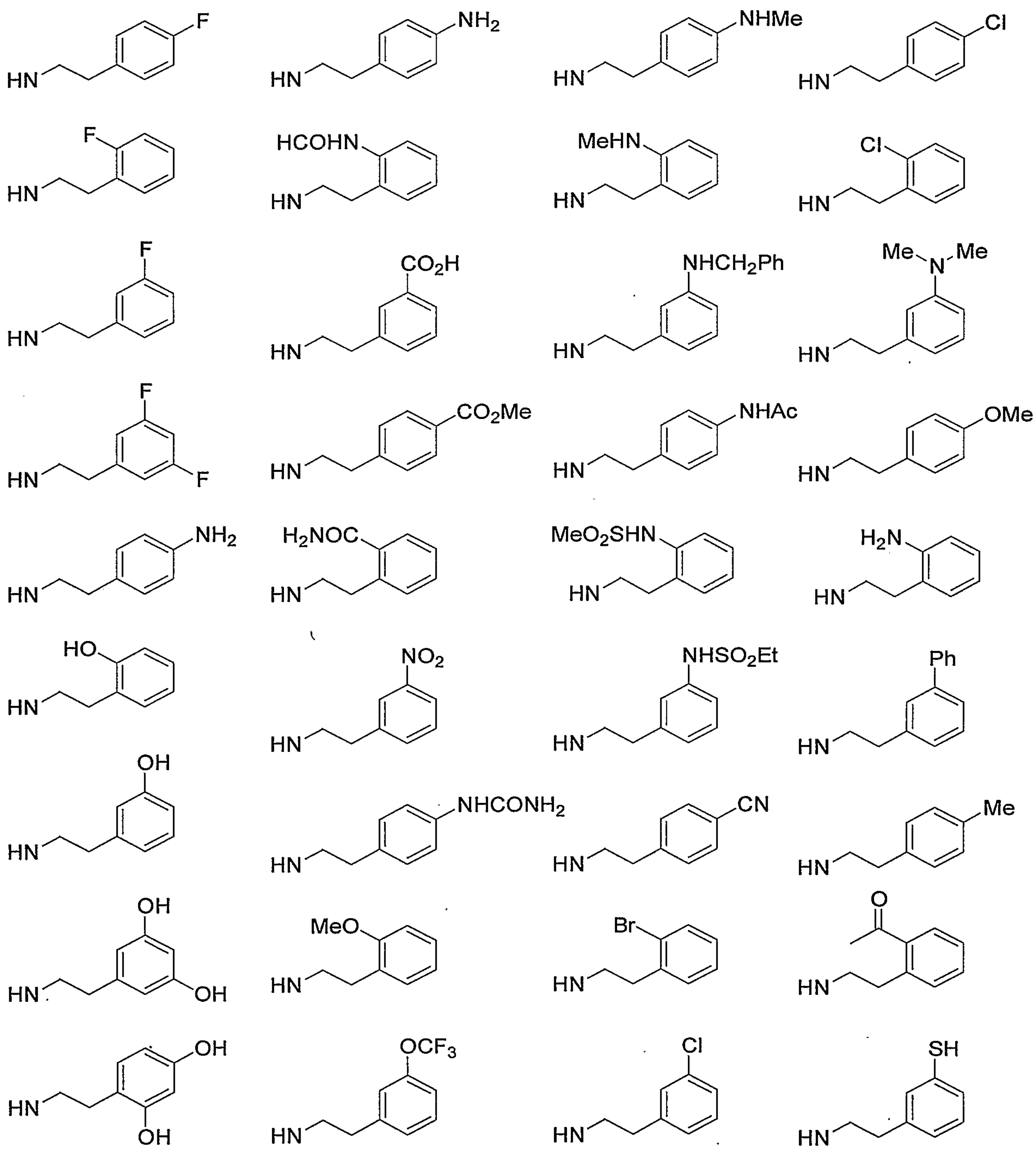

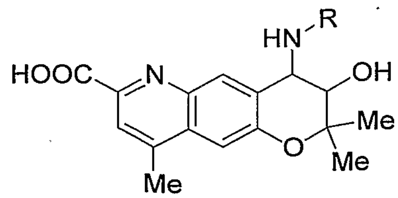

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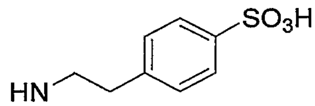	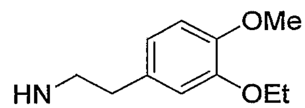	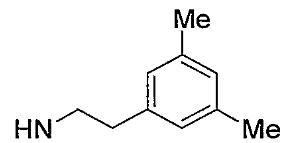
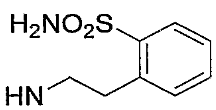	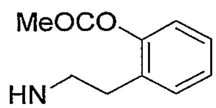	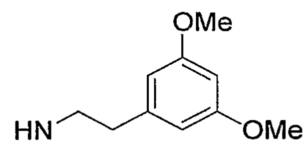
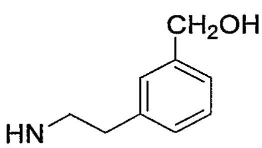	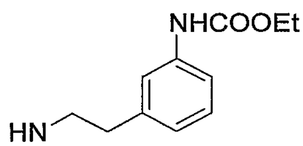	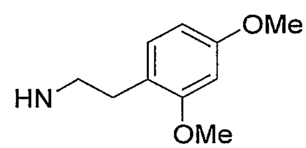
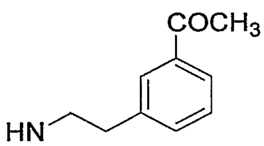	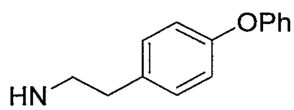	
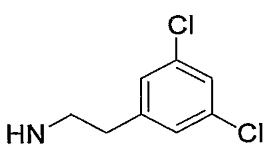	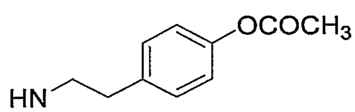	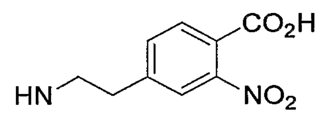
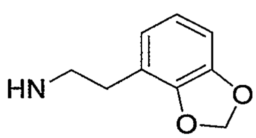	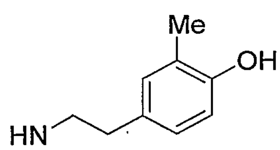	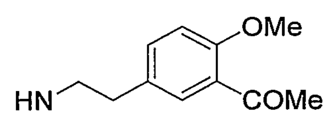
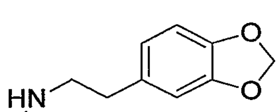	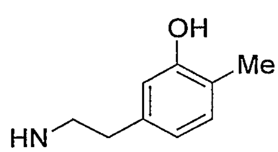	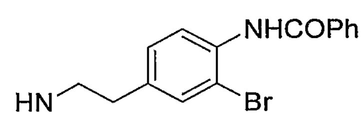
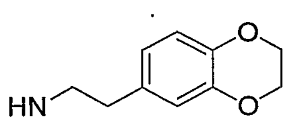	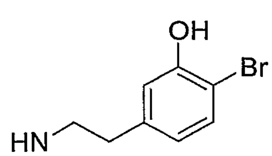	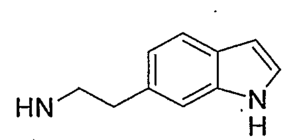

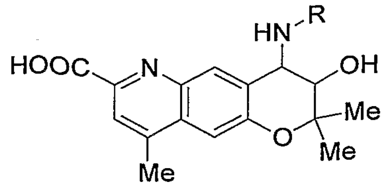

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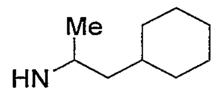
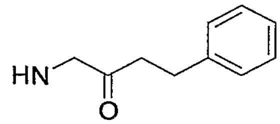
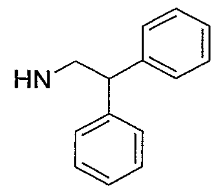
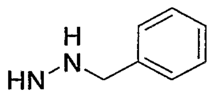
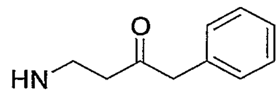
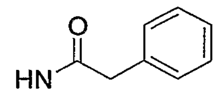
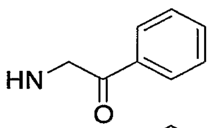
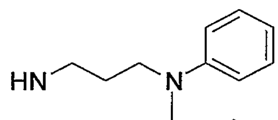
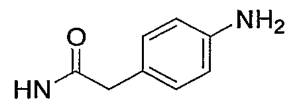
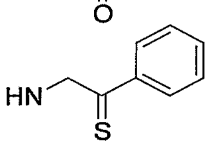
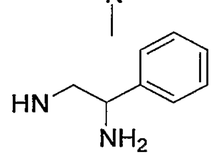
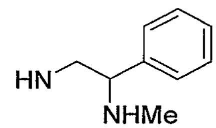
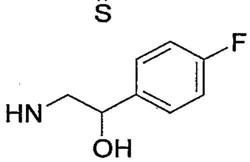
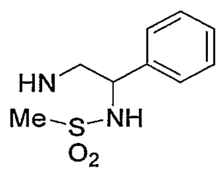
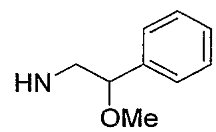
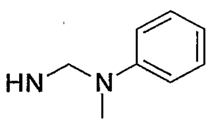
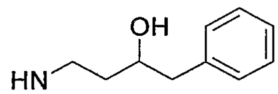
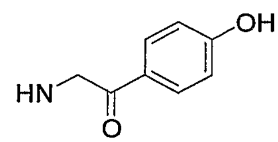
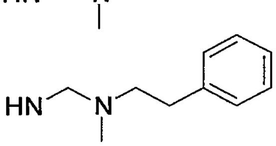
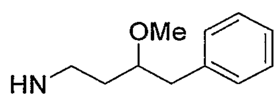
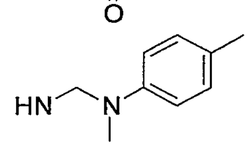
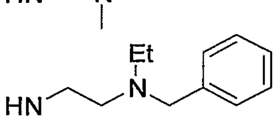
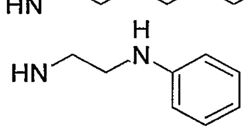
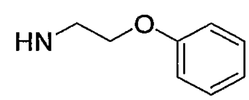
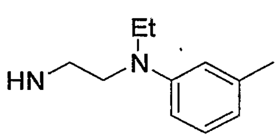
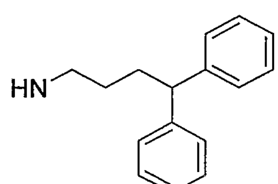
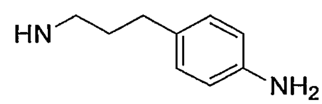
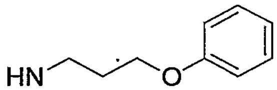
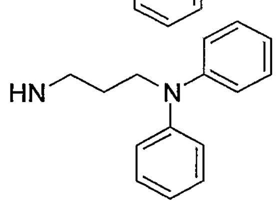
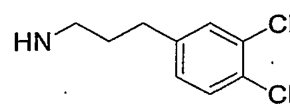
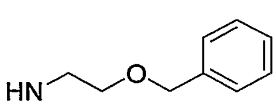

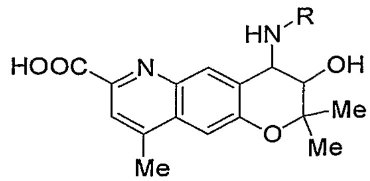

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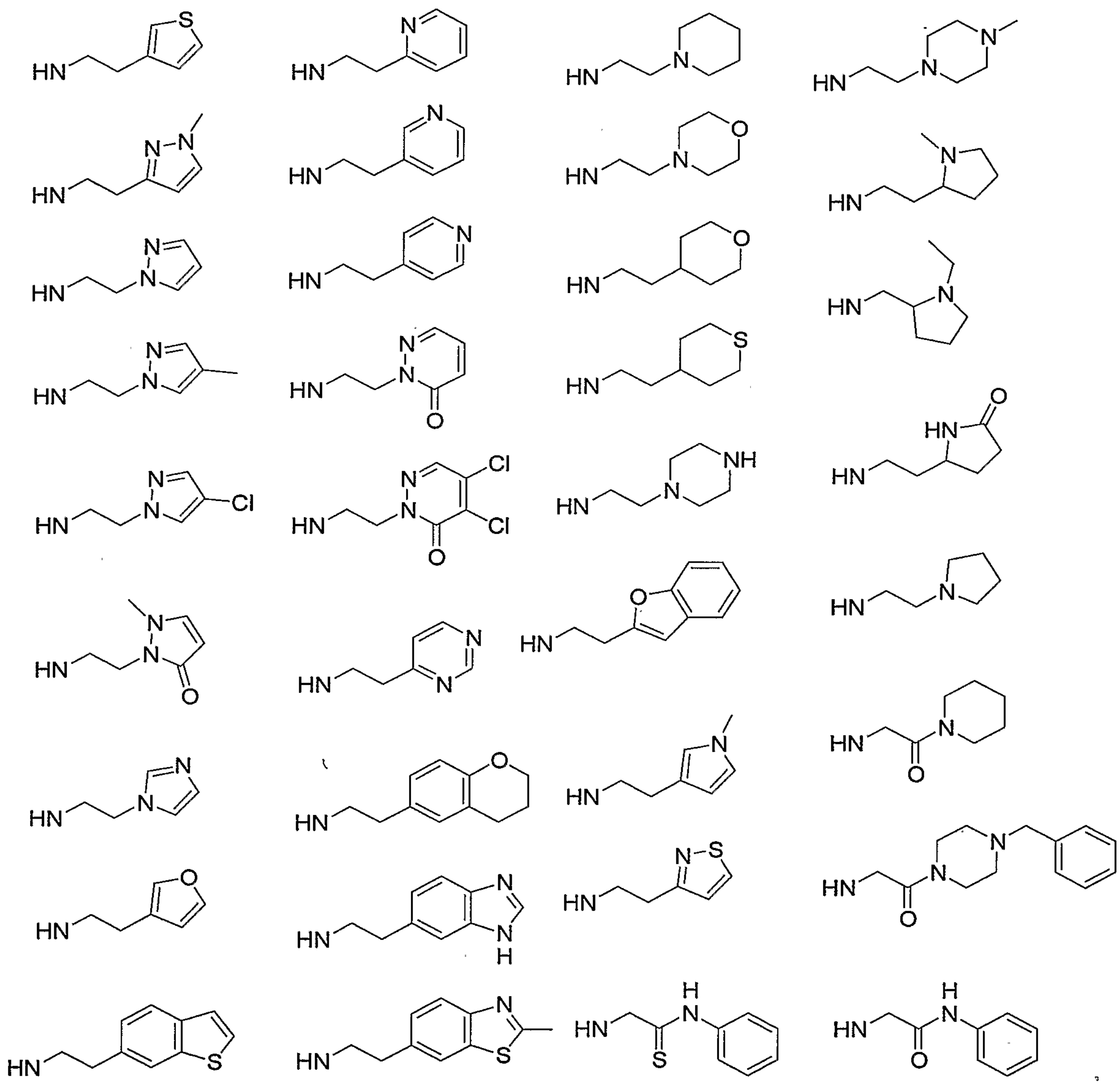

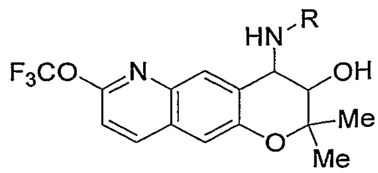

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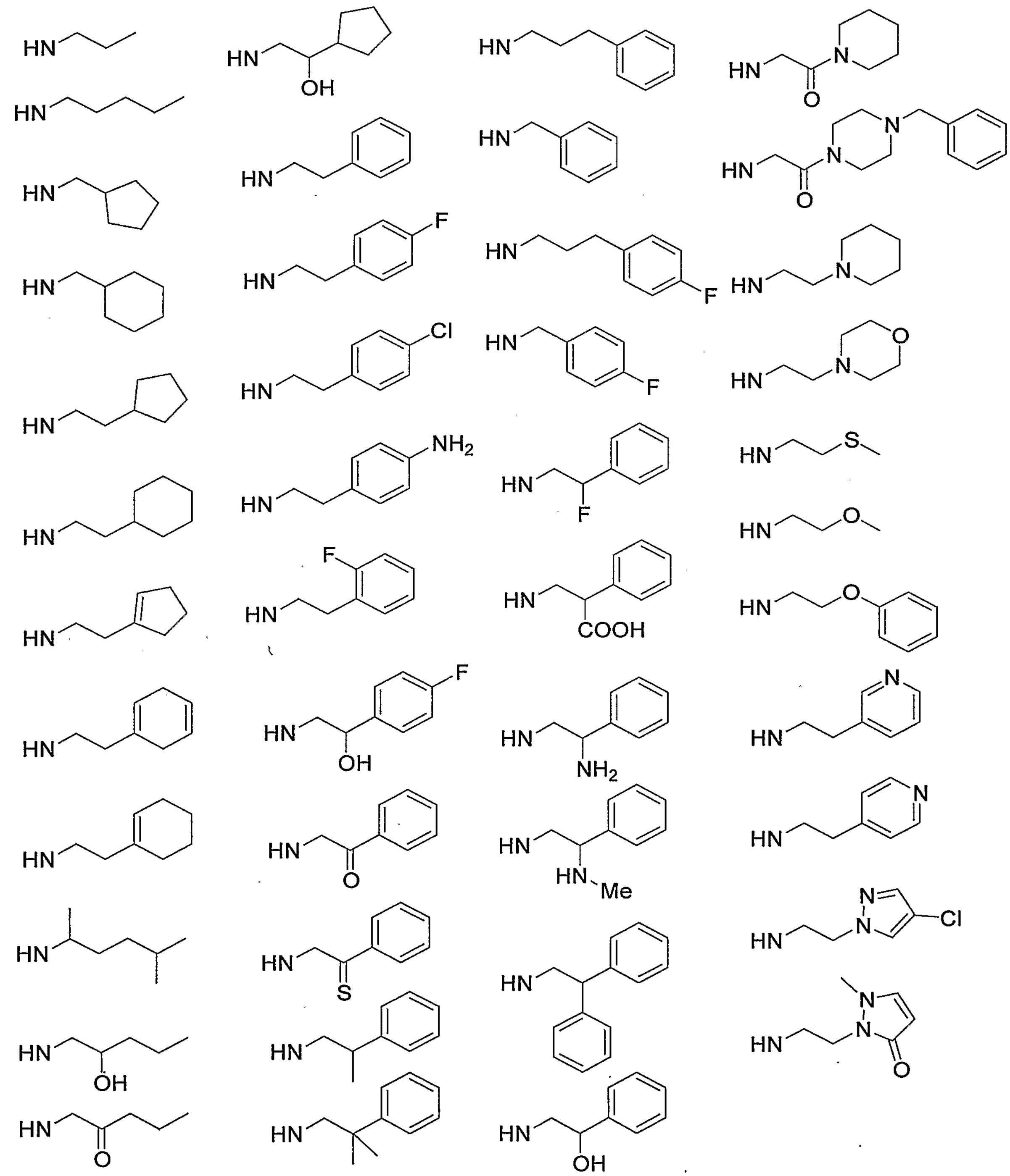

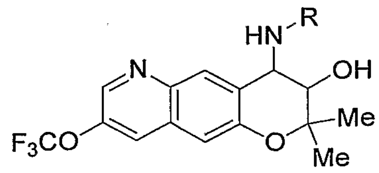

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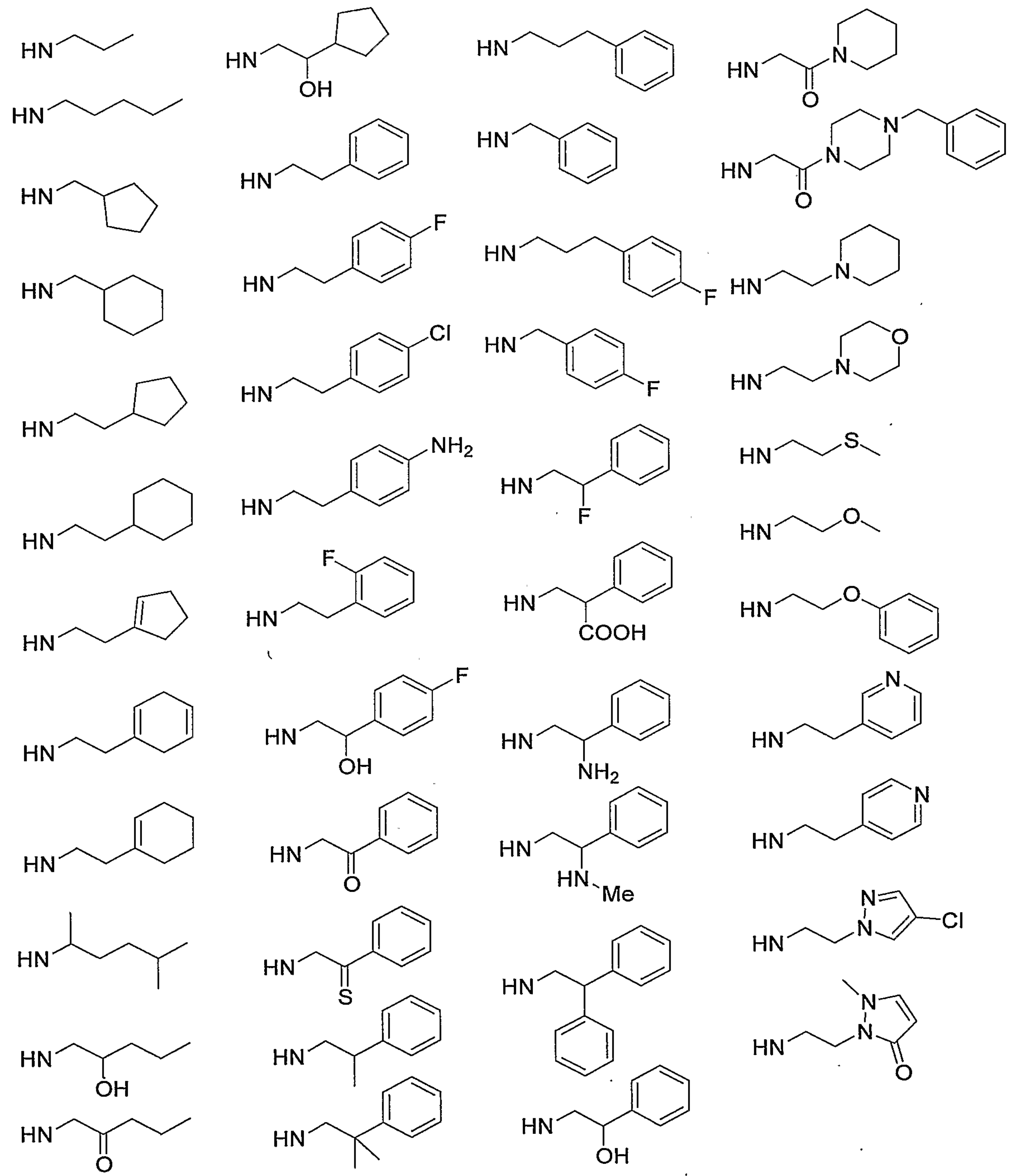
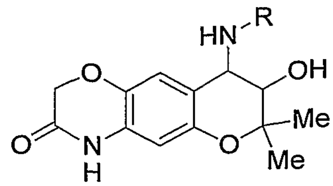
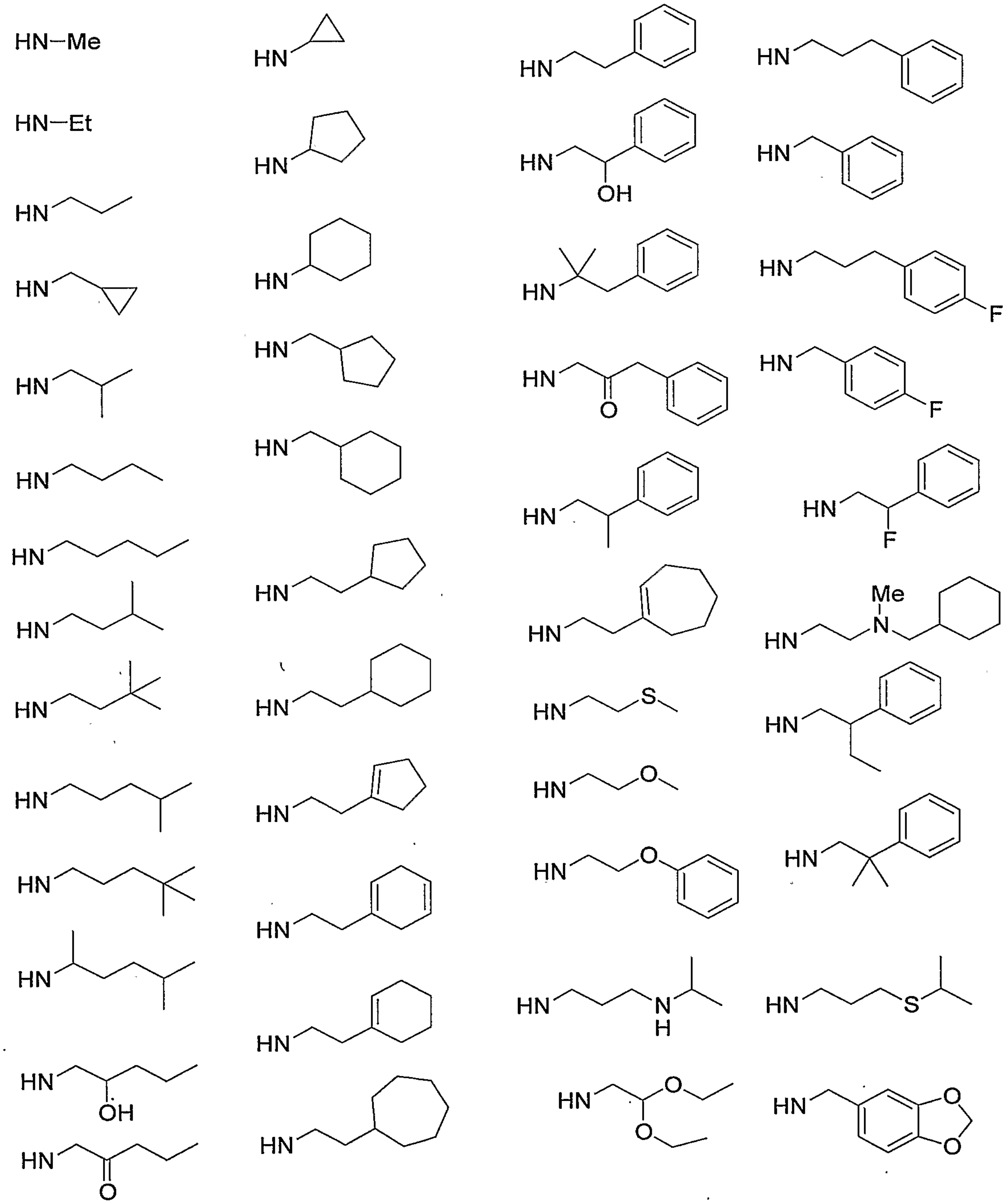


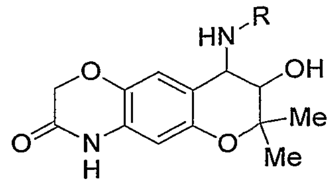


HN—R

HN—Me

HN—Et





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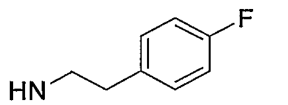
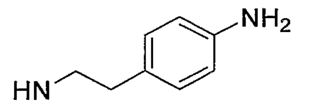
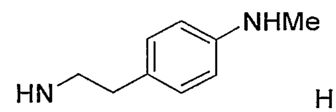
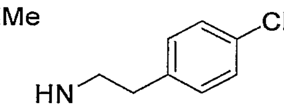
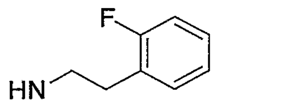
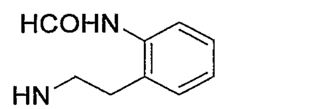
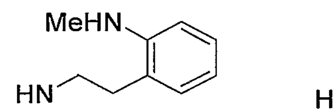
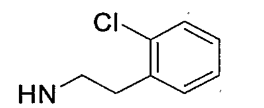
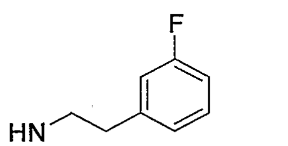
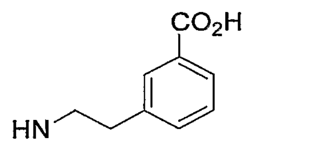
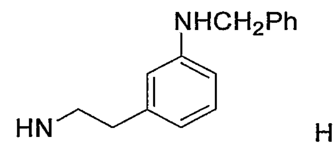
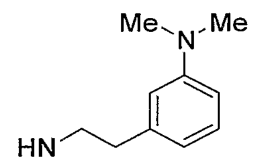
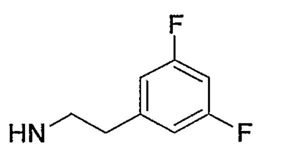
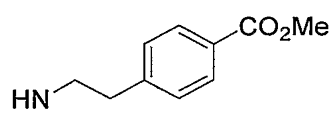
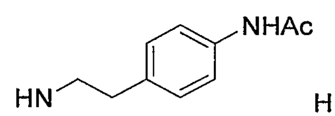
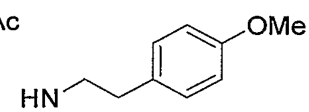
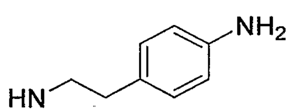
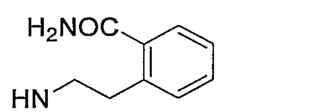
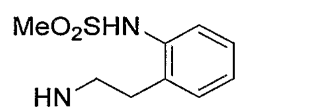
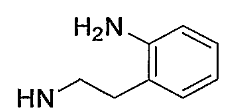
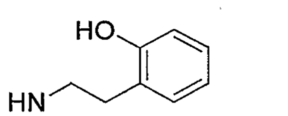
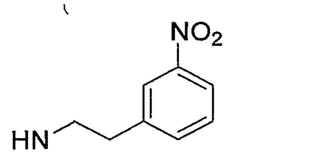
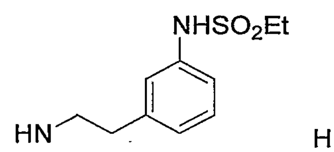
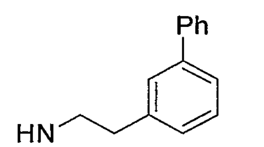
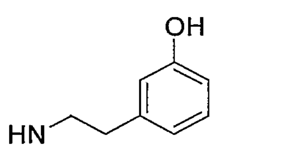
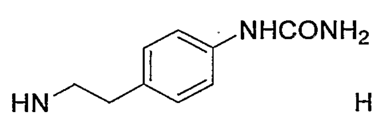
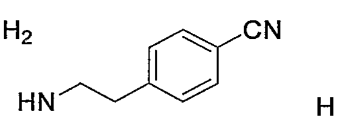
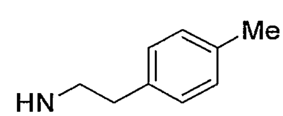
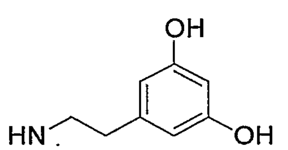
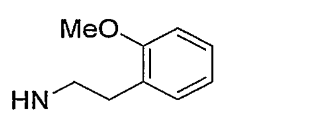
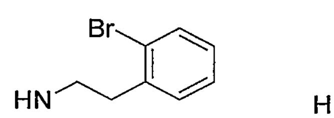
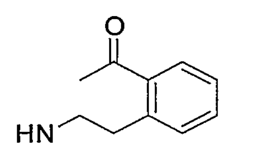
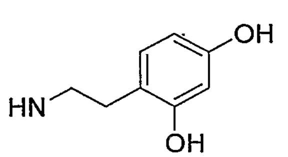
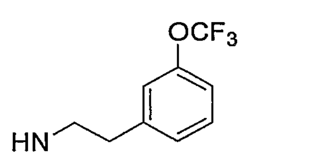
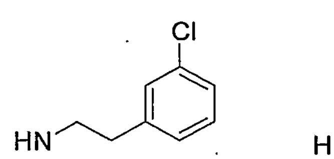
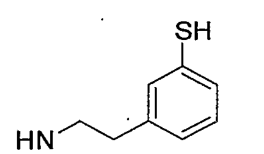
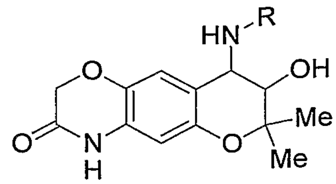
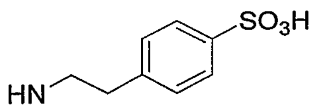
			
			
			
			
			
			
			
			
			


HN R
OH
Me
Me
O
O
N
H
O

HN—R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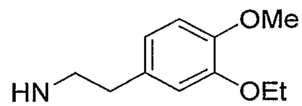
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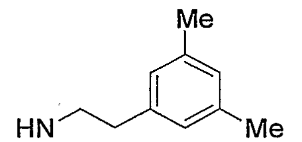
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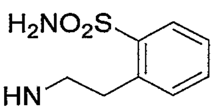
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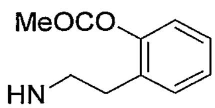
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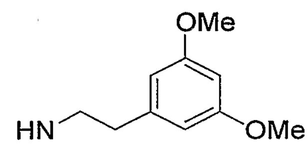
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OMe
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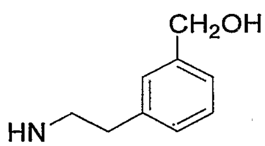
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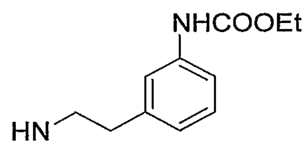
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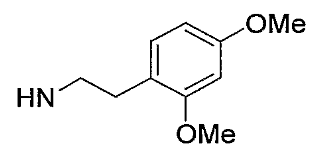
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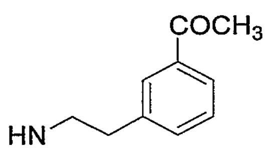
OMe
HN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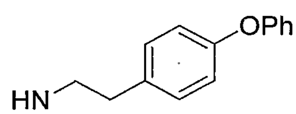
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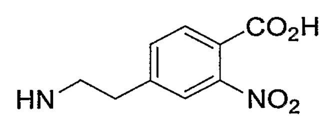
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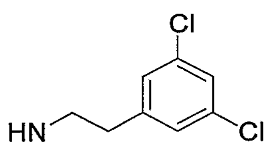
NO_2
HN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Cl
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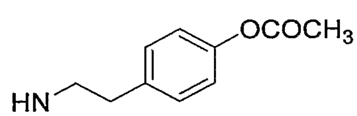
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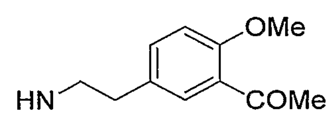
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COMe
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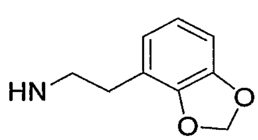
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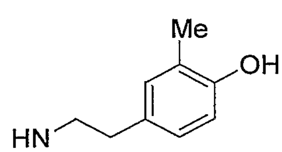
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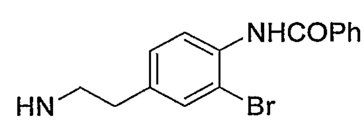
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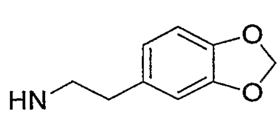
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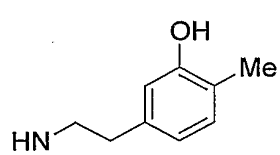
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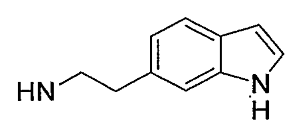
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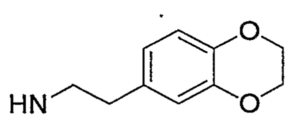
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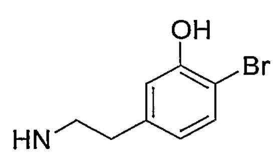
OH
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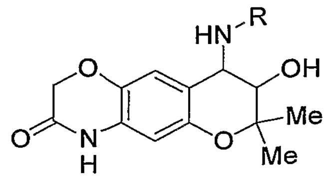

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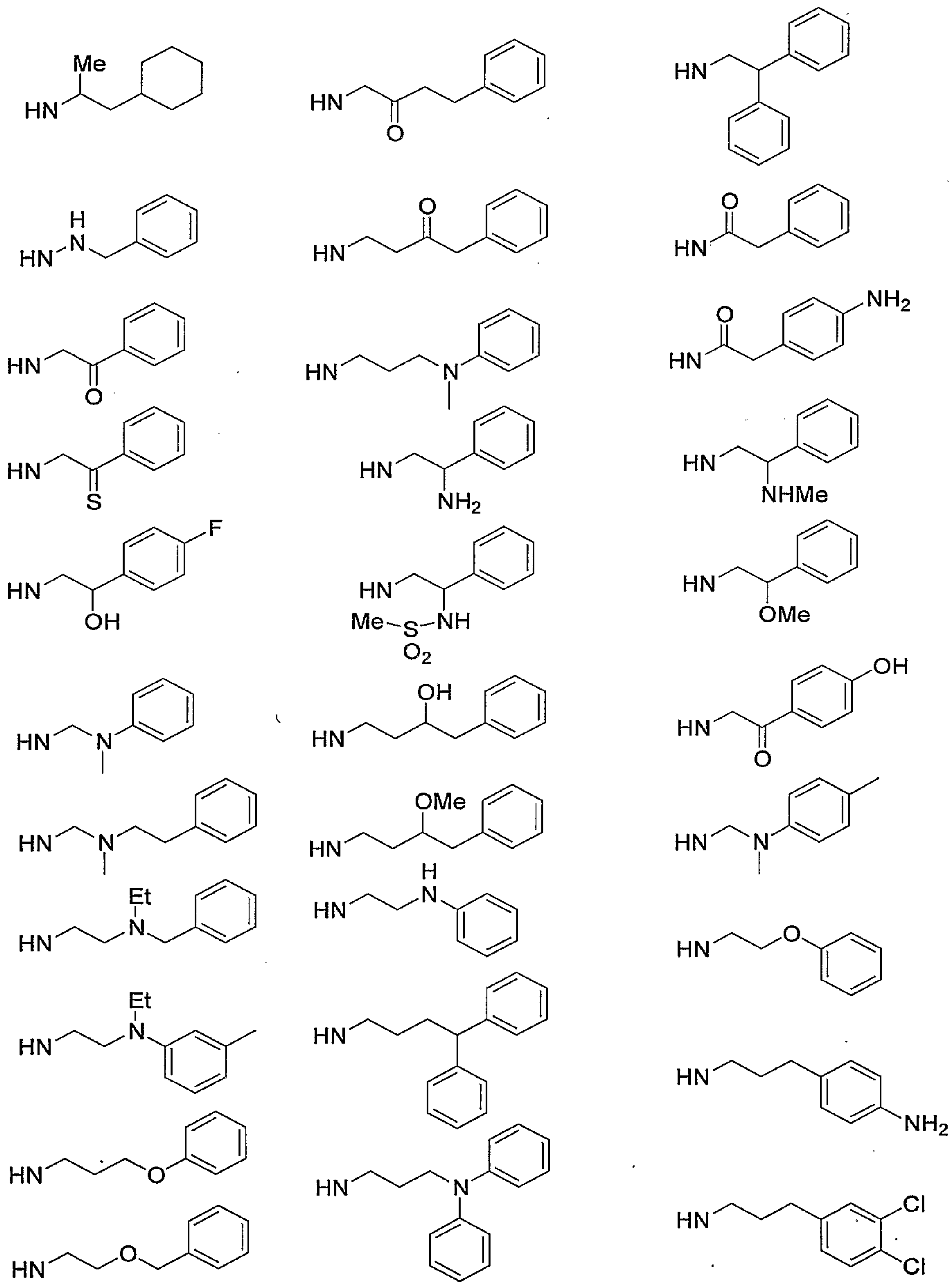

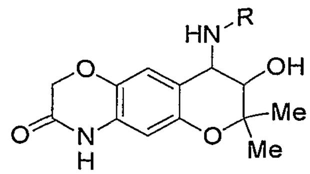

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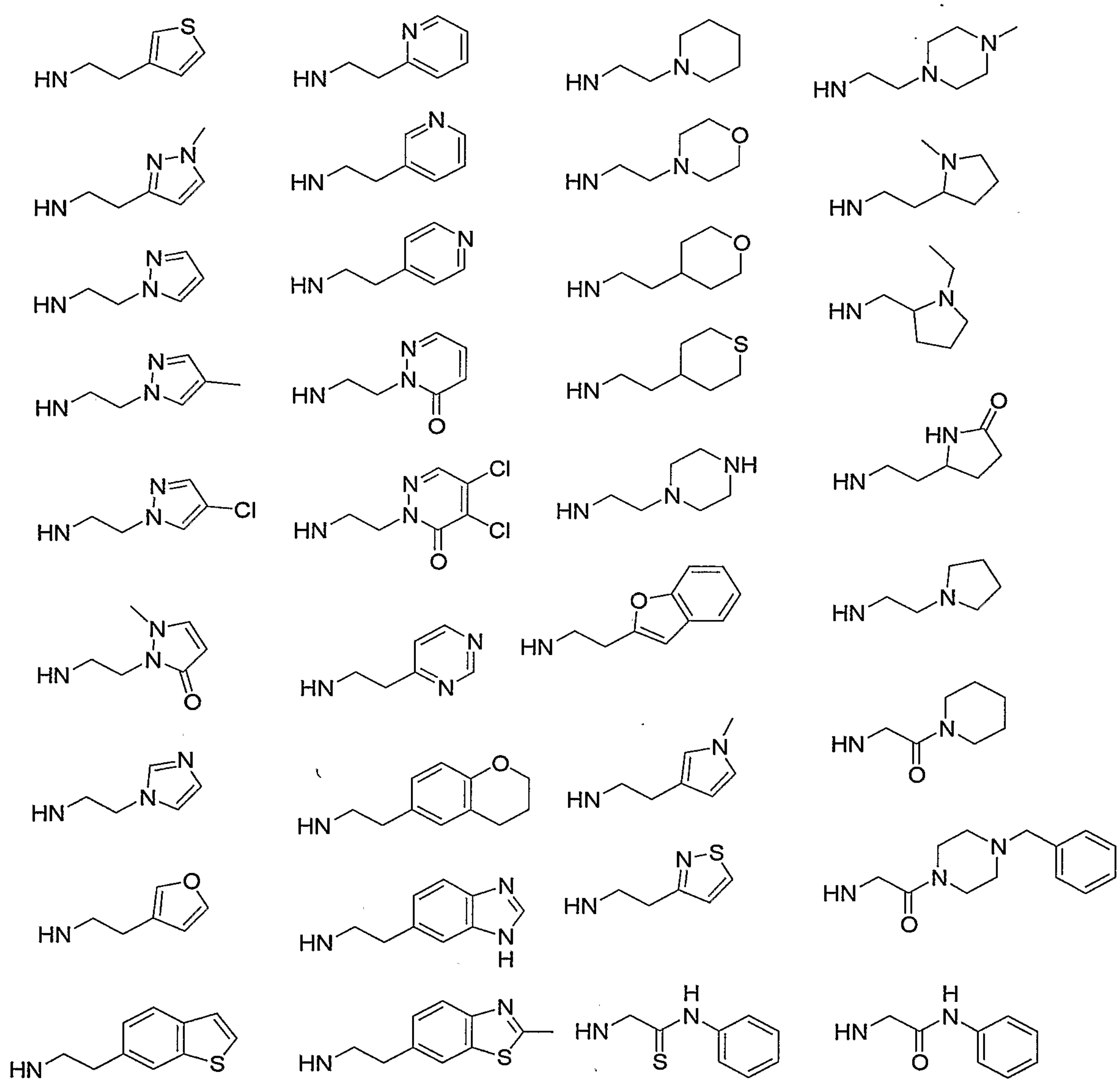

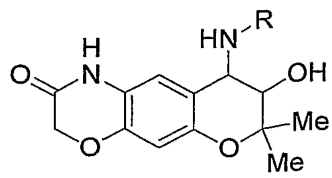

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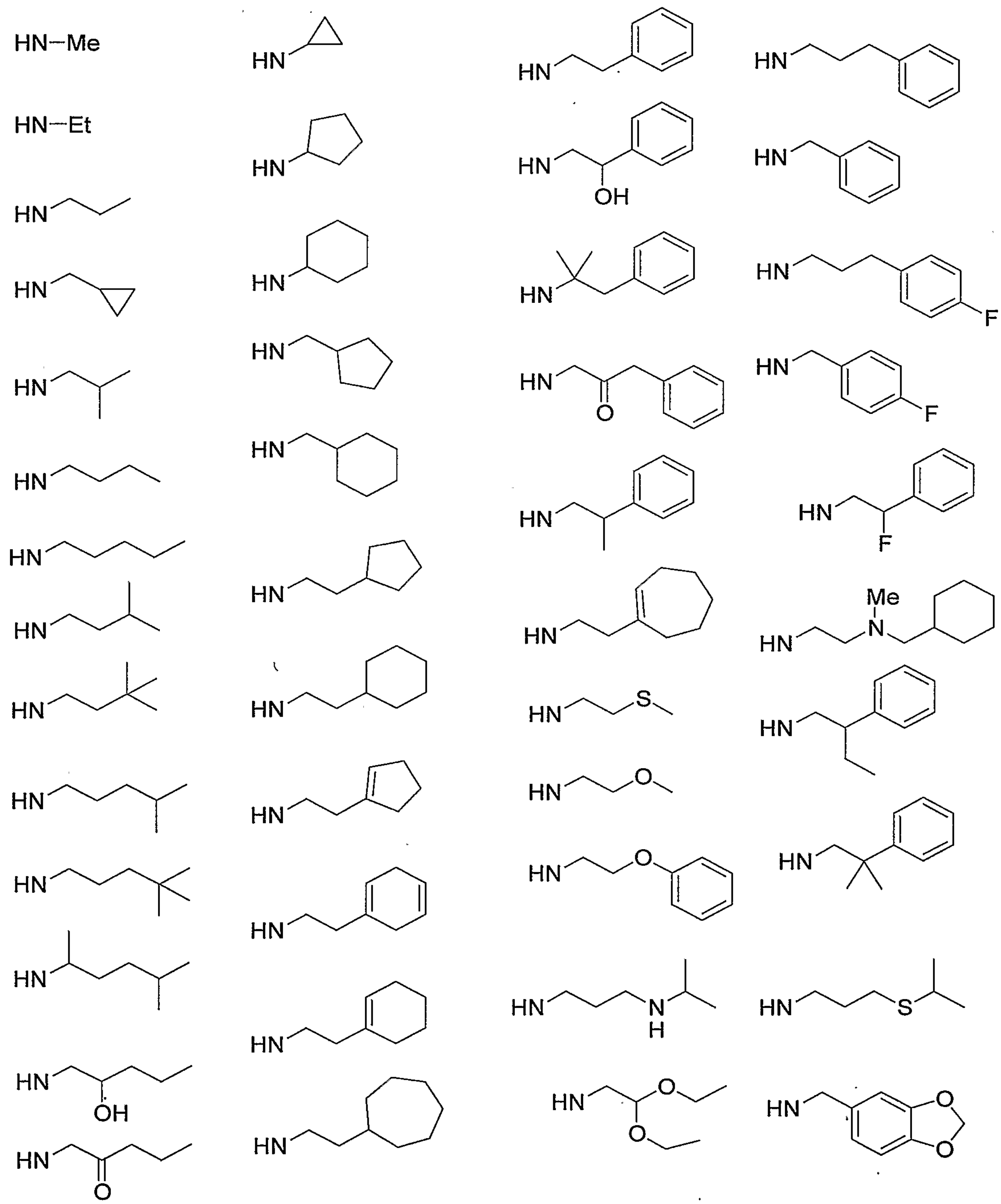

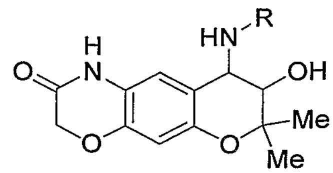

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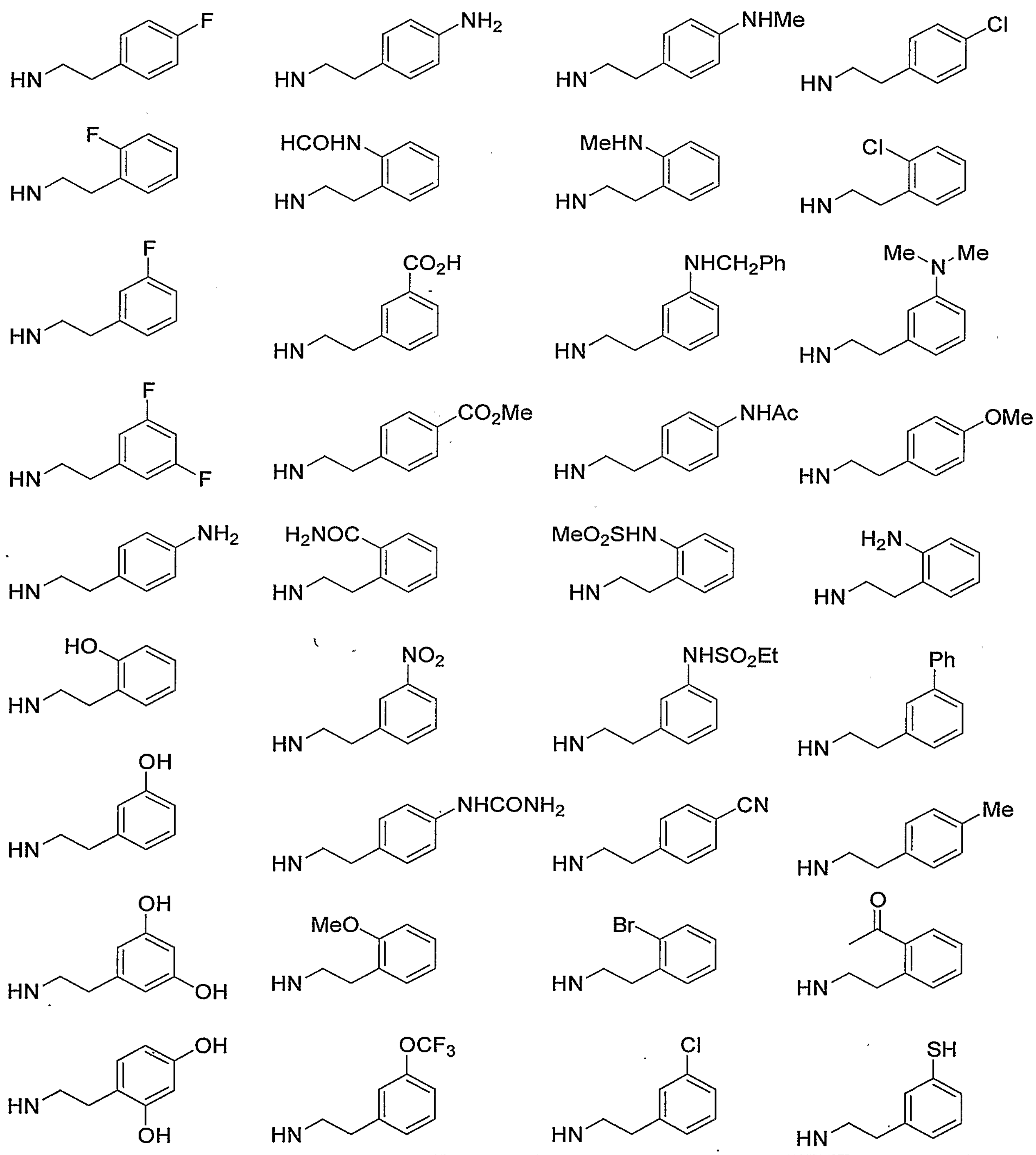

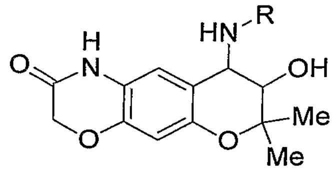

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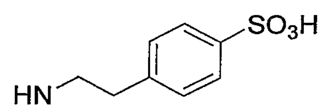	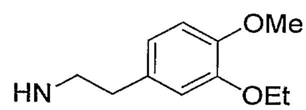	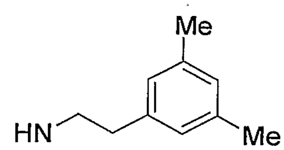
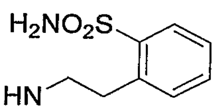	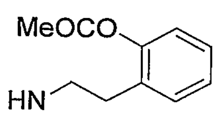	
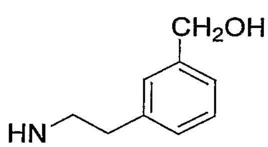	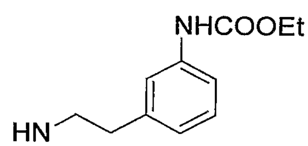	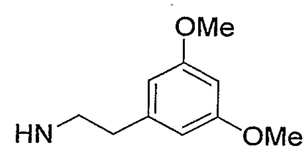
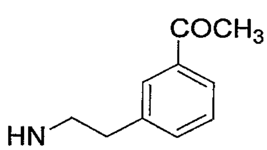	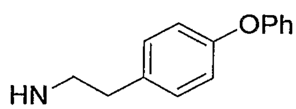	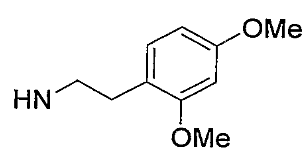
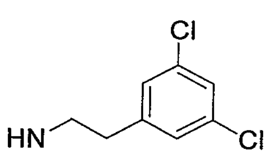	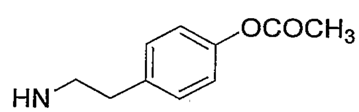	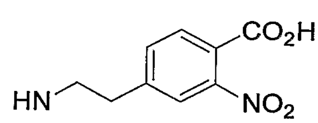
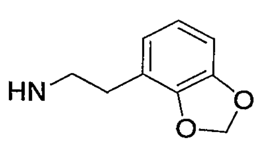	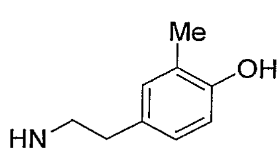	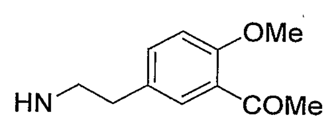
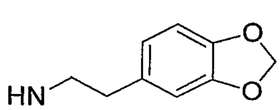	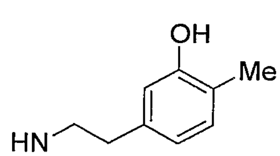	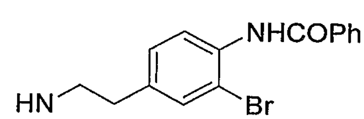
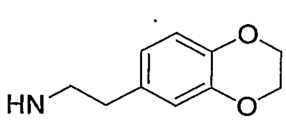	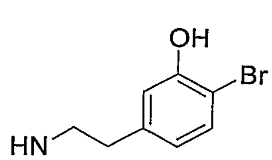	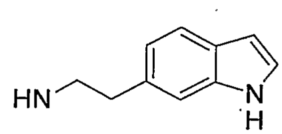

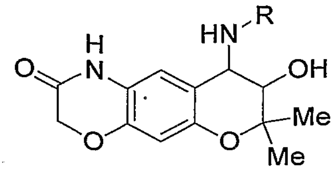

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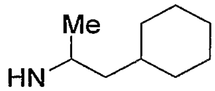
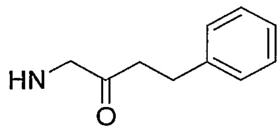
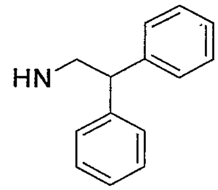
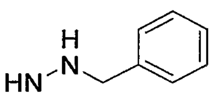
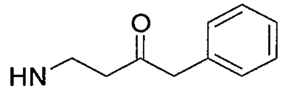
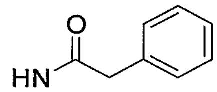
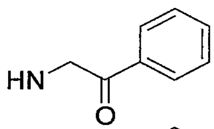
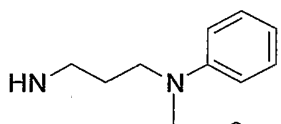
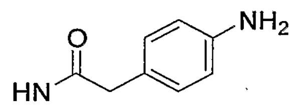
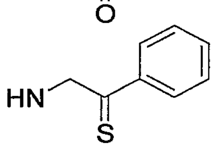
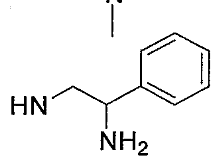
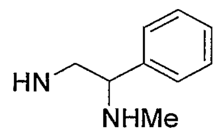
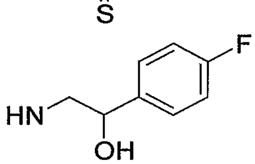
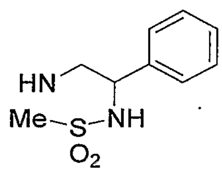
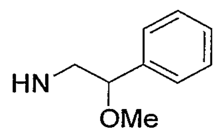
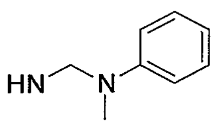
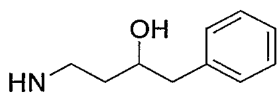
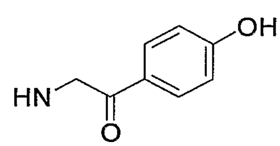
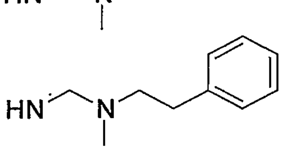
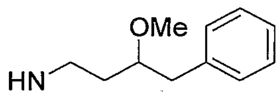
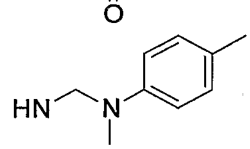
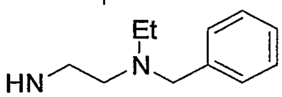
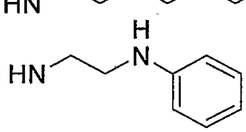
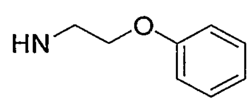
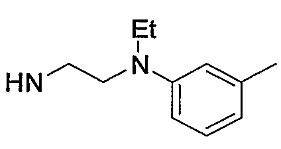
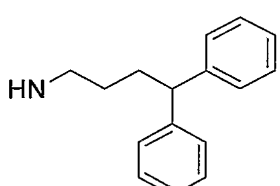
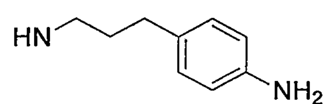
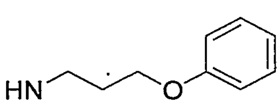
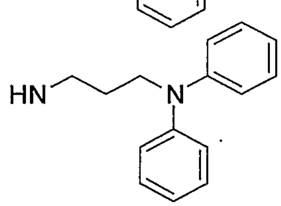
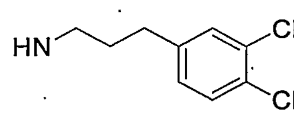
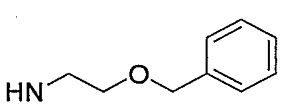

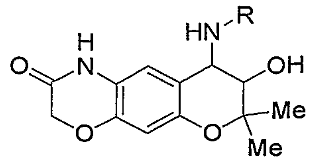

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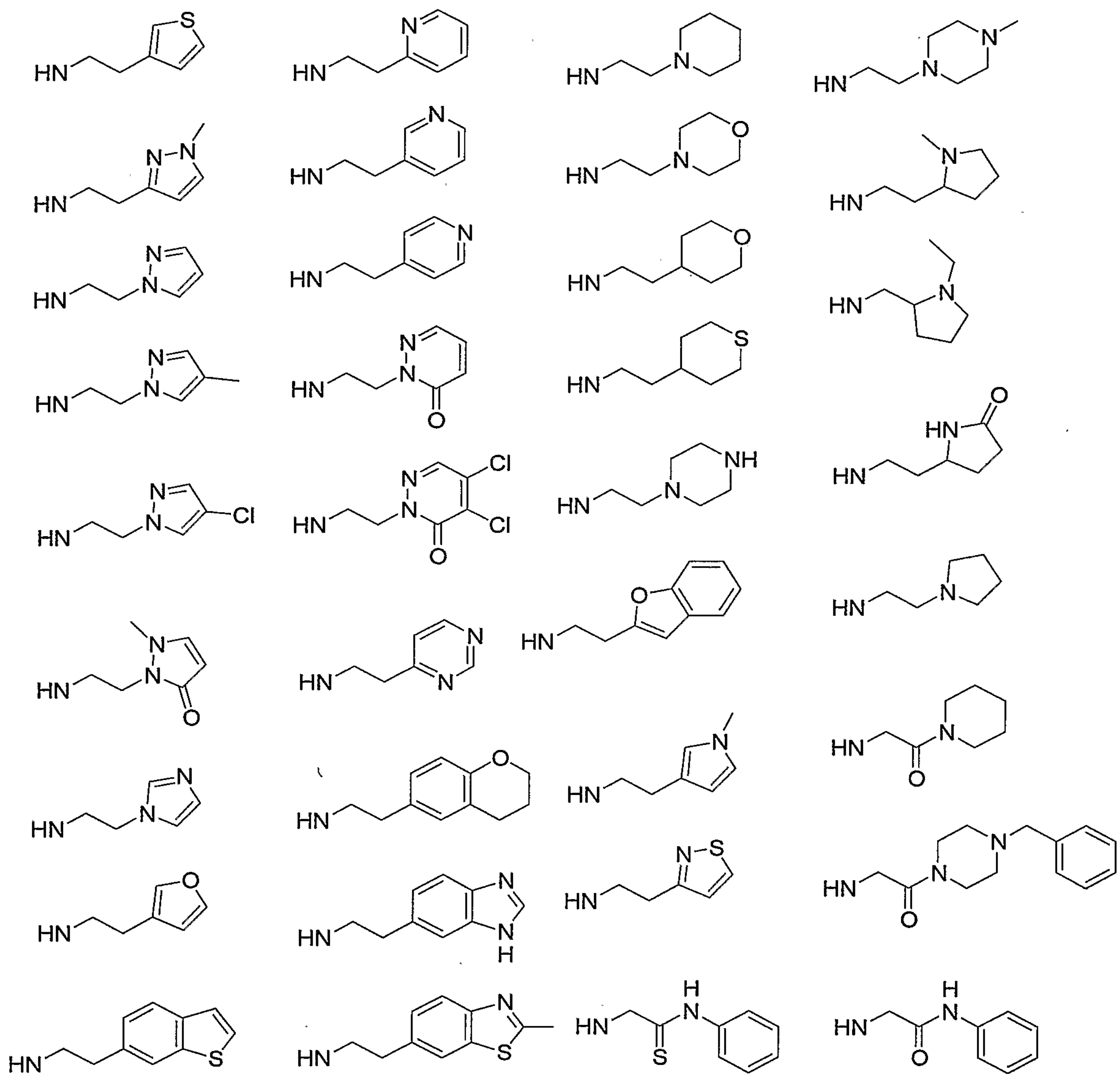

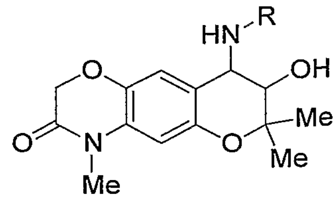

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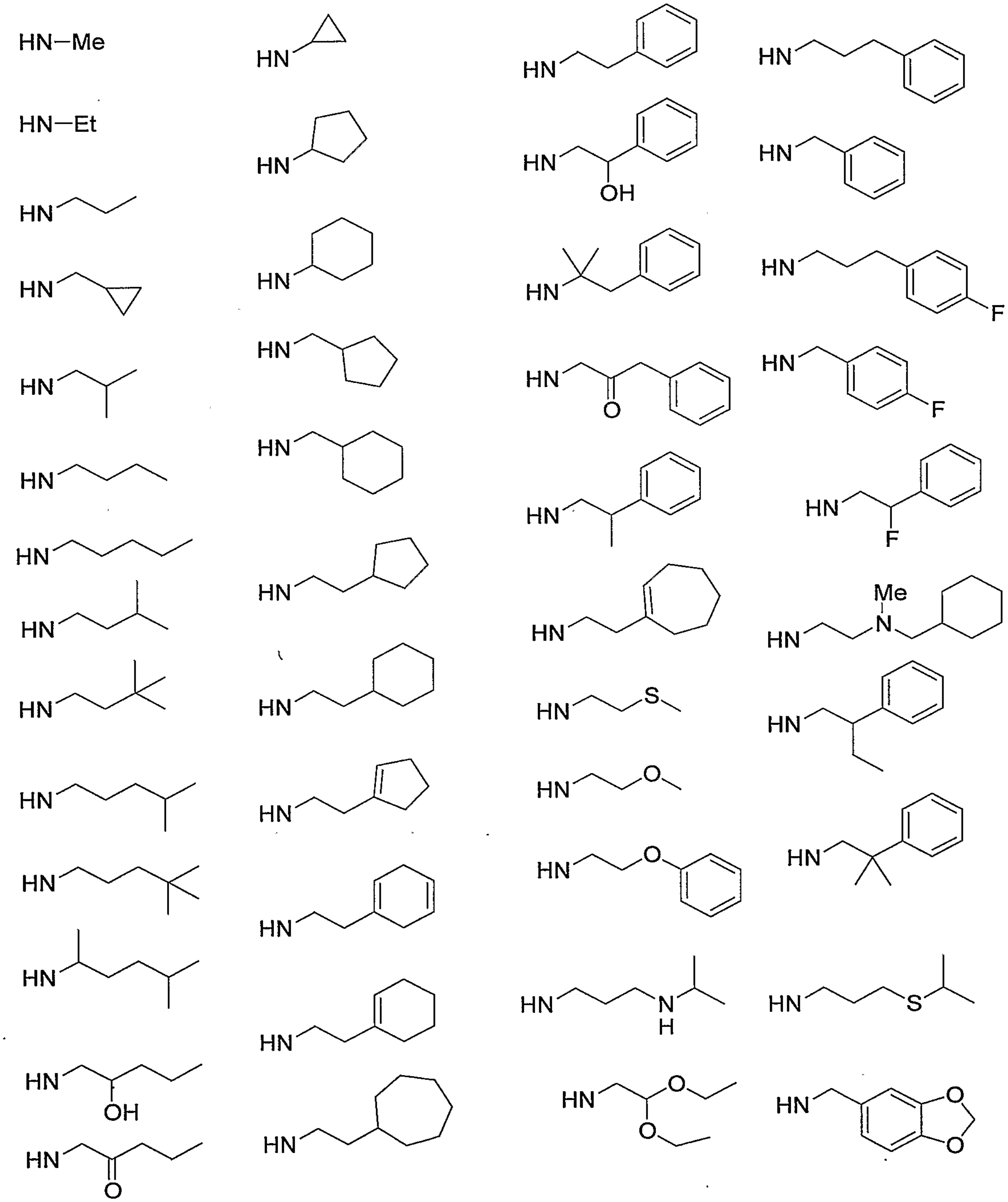

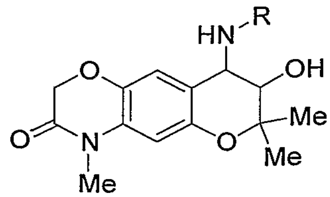

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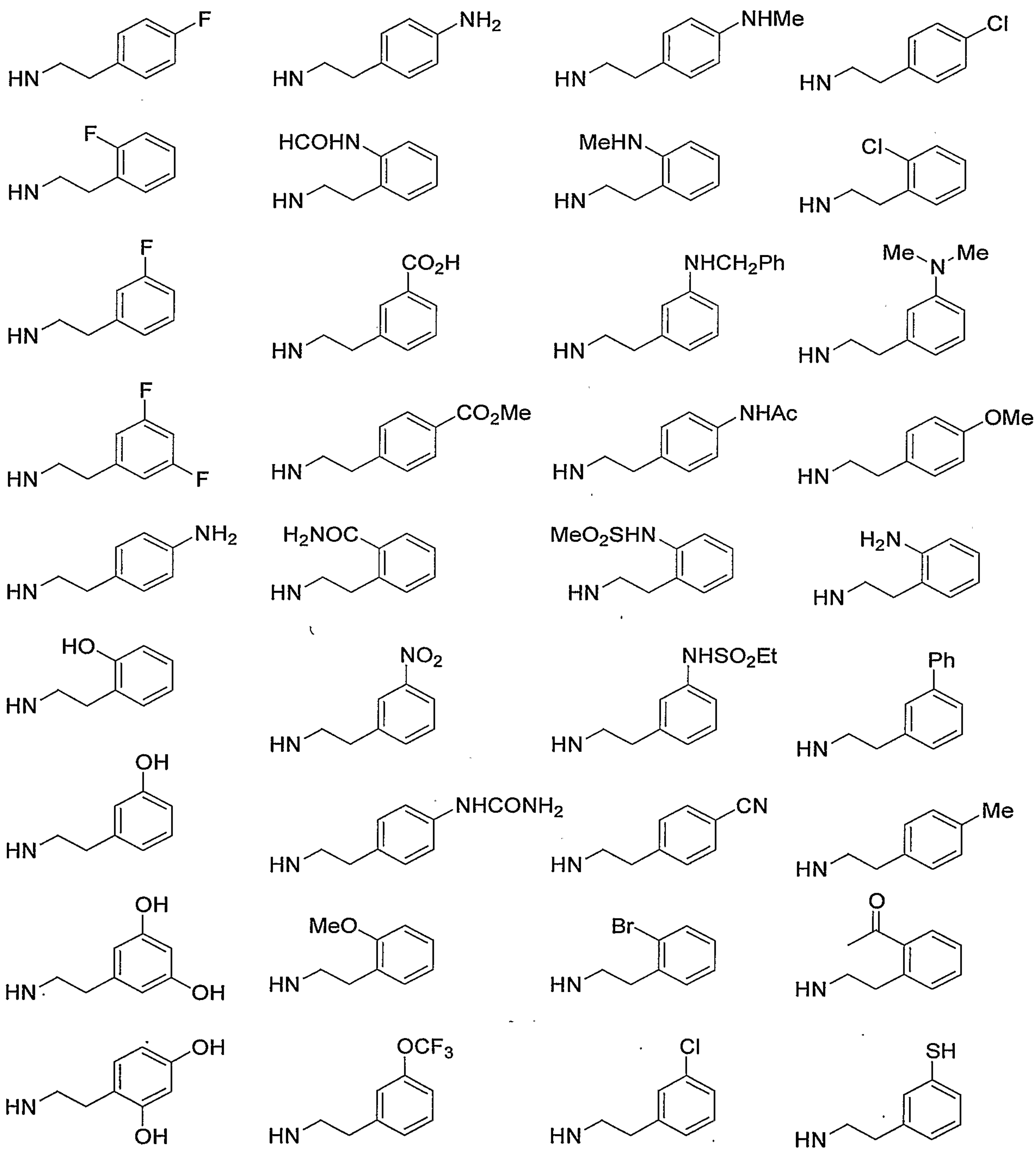

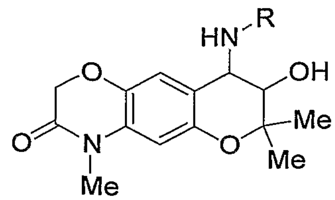

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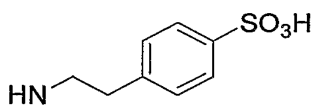	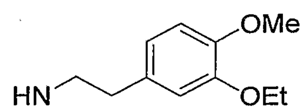	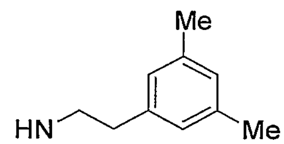
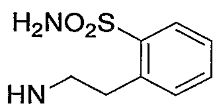	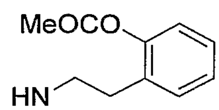	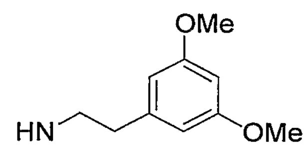
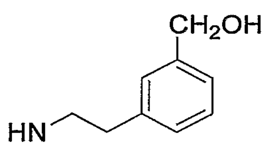	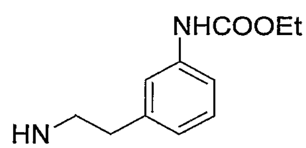	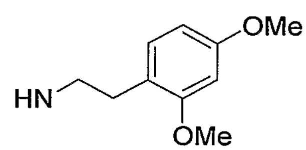
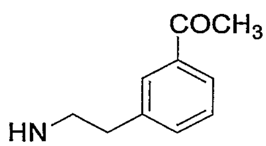	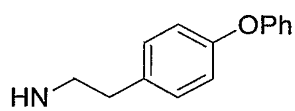	
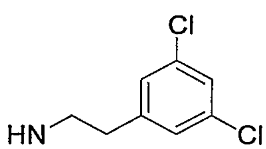	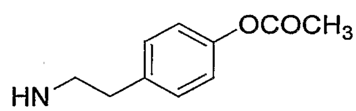	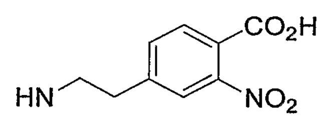
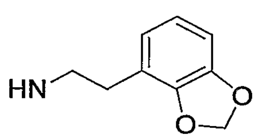	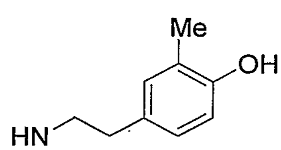	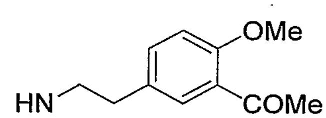
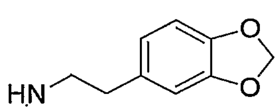	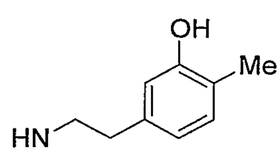	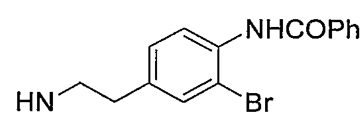
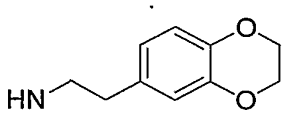	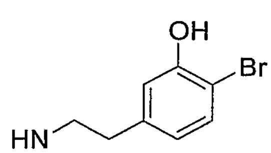	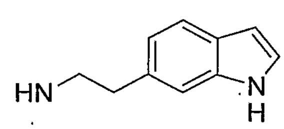

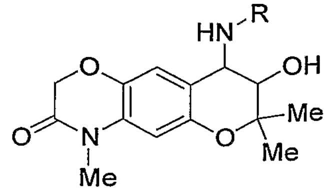

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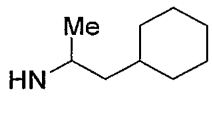
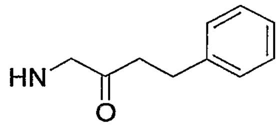
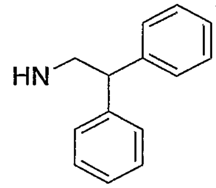

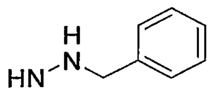
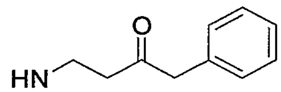
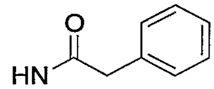

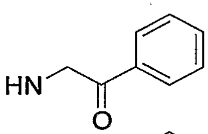
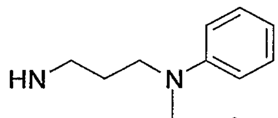
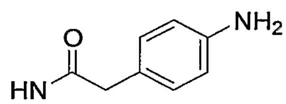

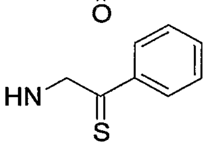
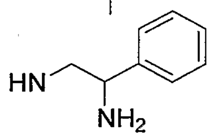
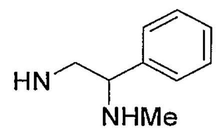

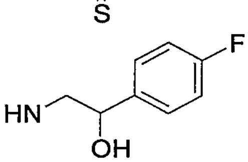
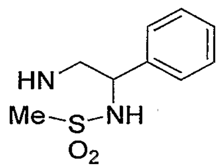
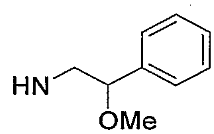

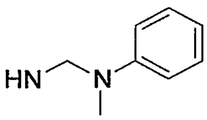
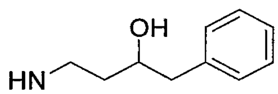
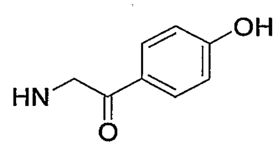

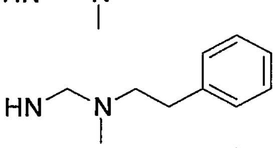
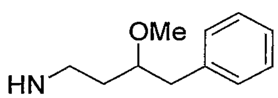
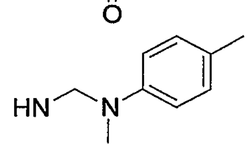

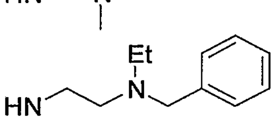
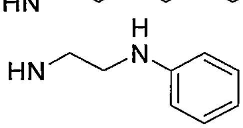
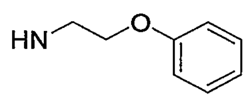

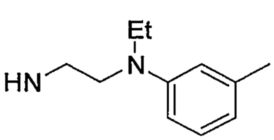
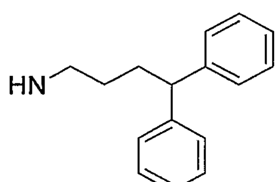
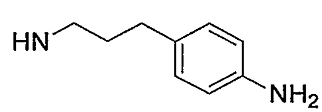

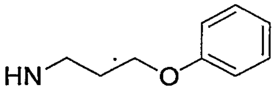
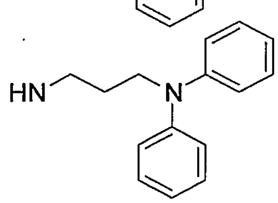
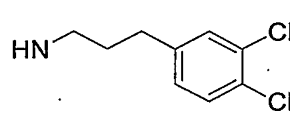

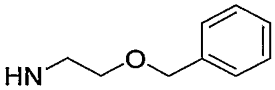

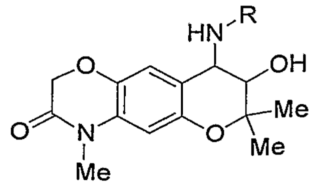

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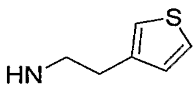	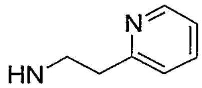	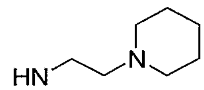	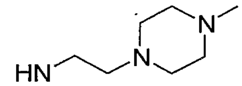
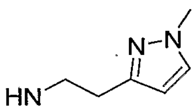	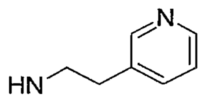	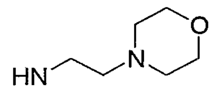	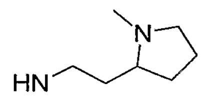
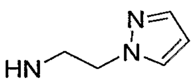	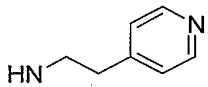	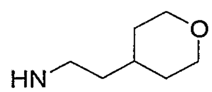	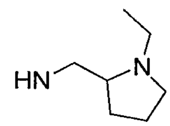
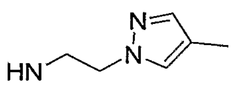	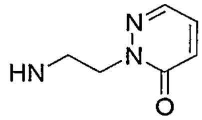	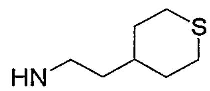	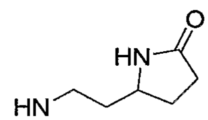
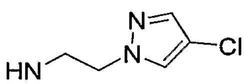	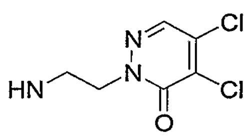	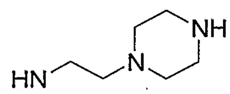	
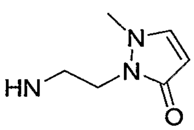	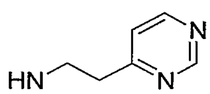	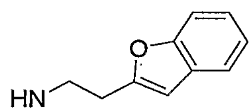	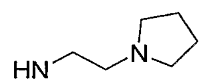
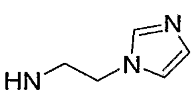	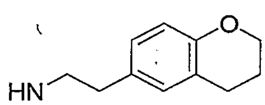	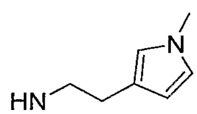	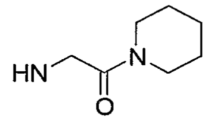
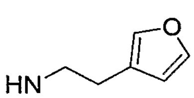	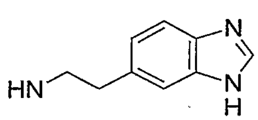	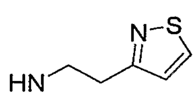	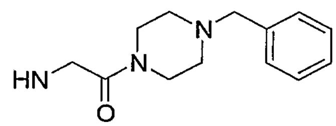
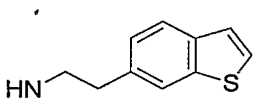	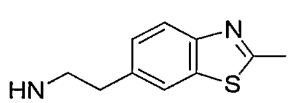	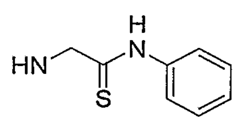	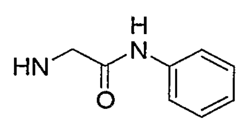

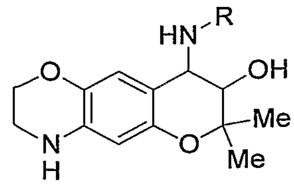

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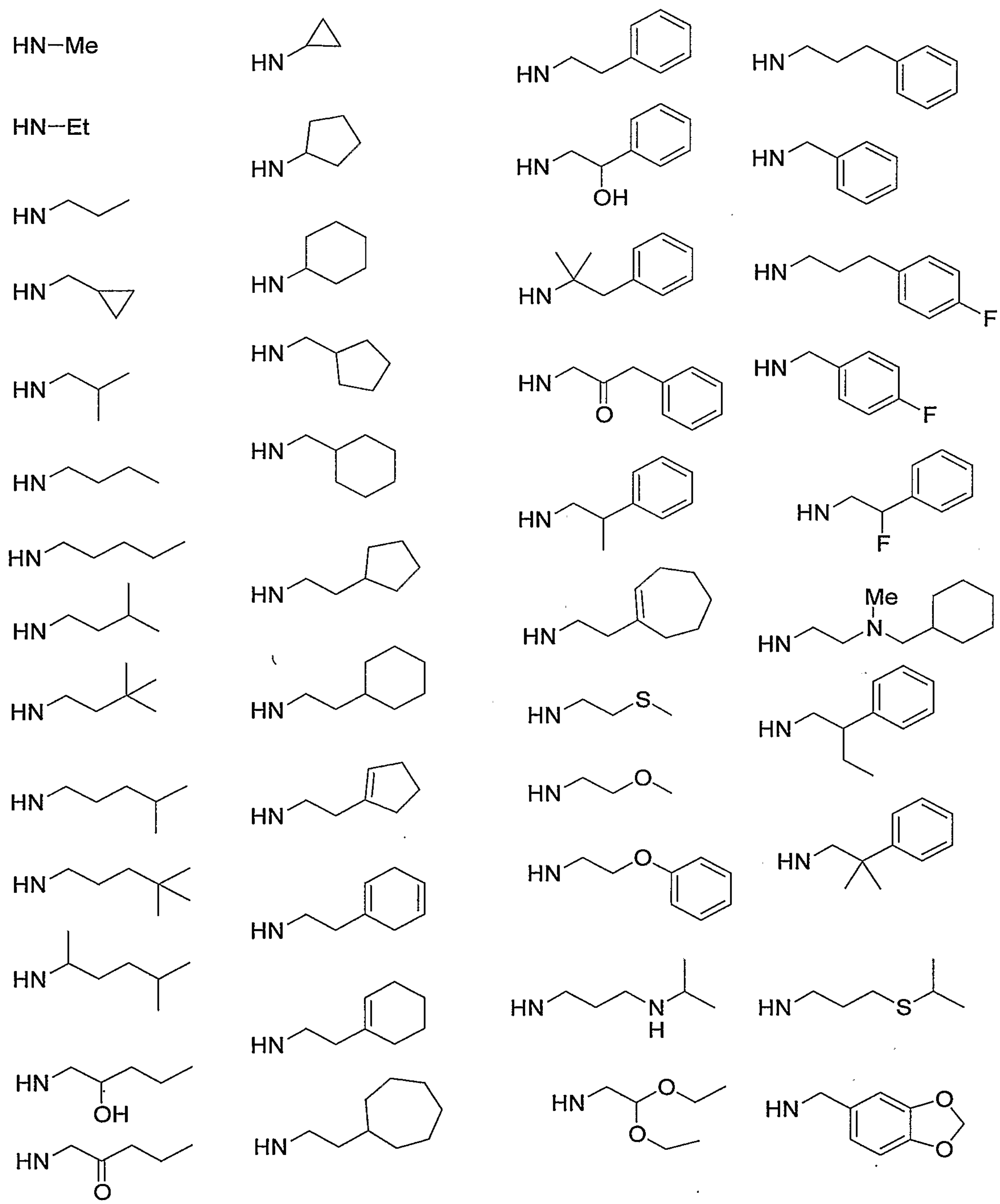

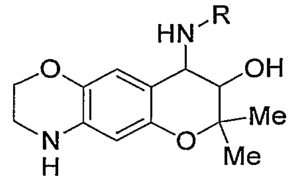

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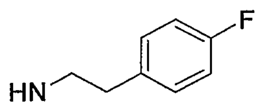	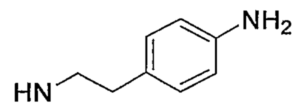	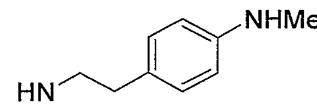	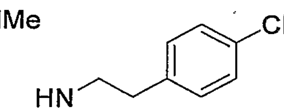
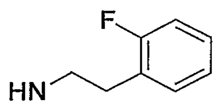	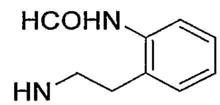	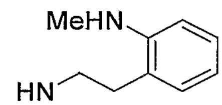	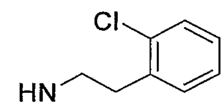
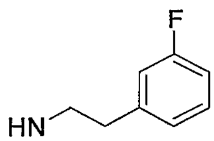	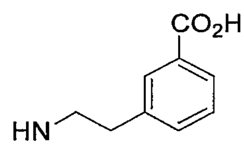	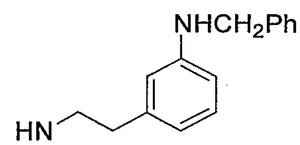	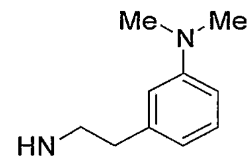
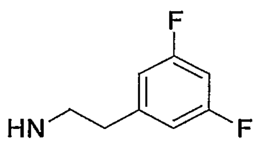	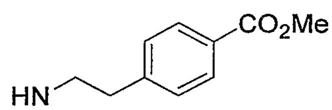	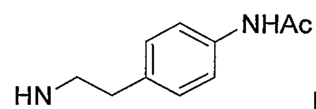	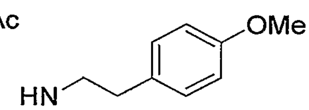
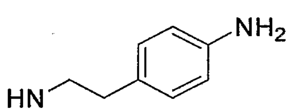	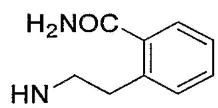	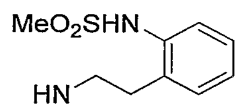	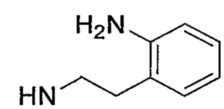
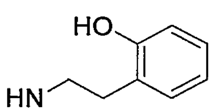	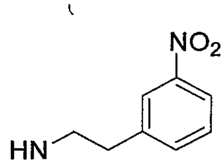	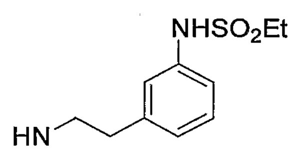	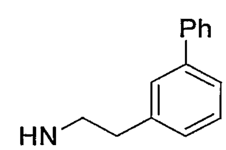
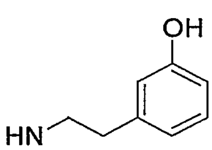	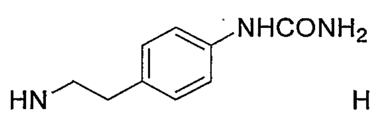	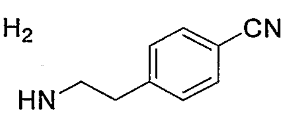	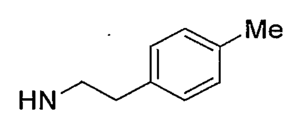
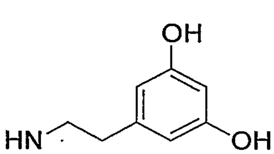	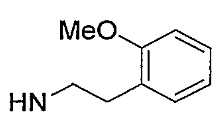	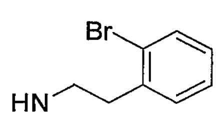	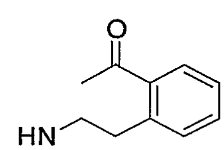
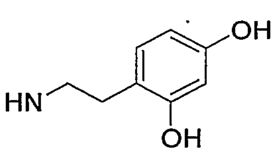	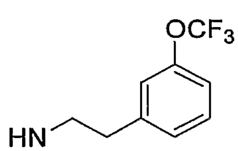	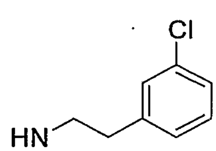	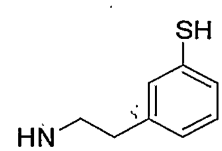

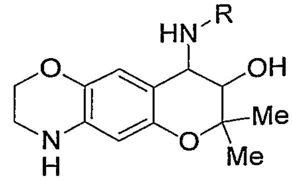

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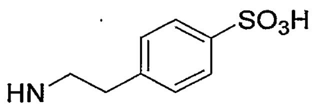	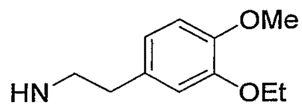	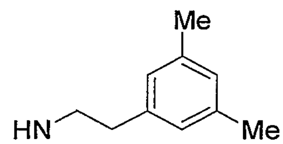
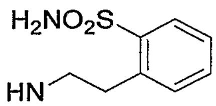	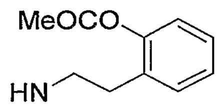	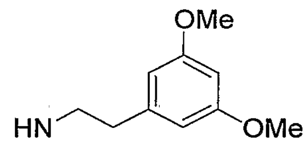
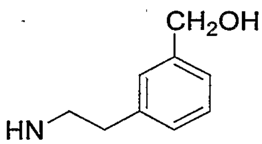	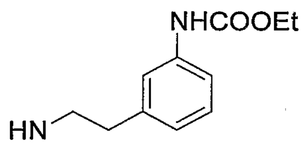	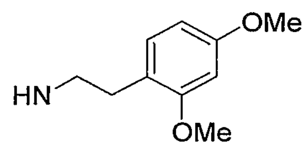
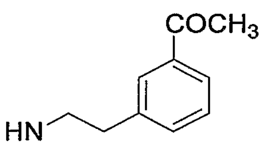	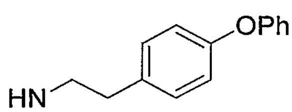	
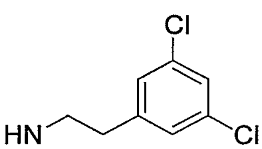	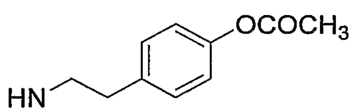	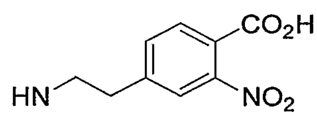
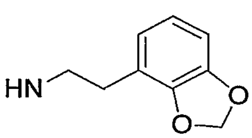	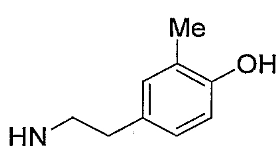	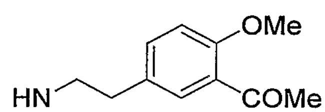
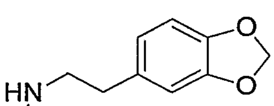	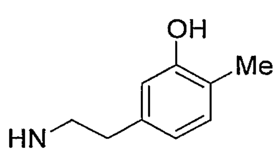	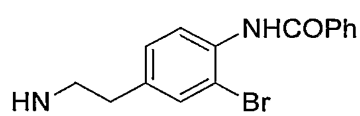
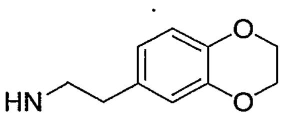	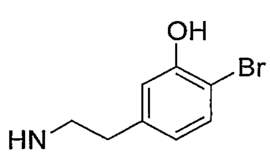	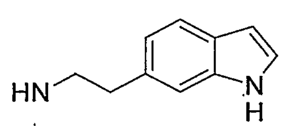

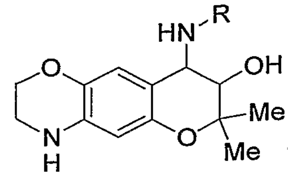

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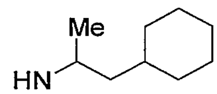	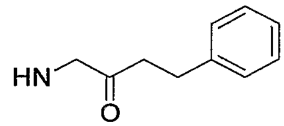	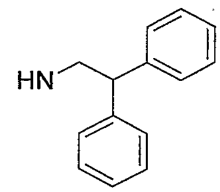
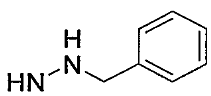	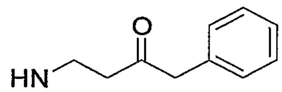	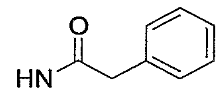
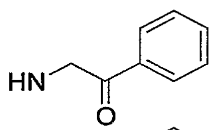	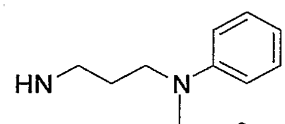	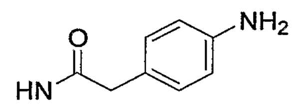
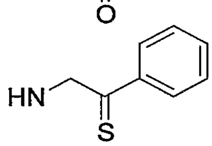	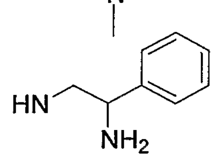	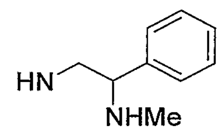
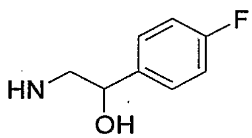	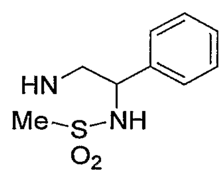	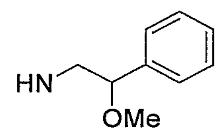
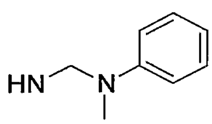	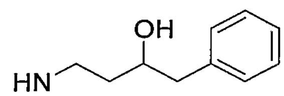	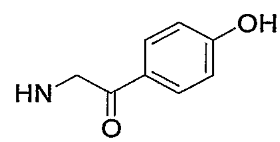
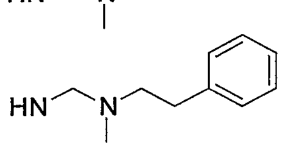	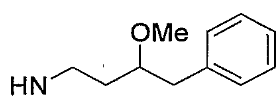	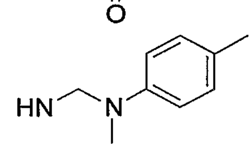
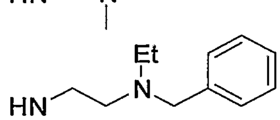	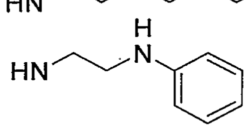	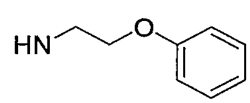
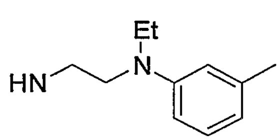	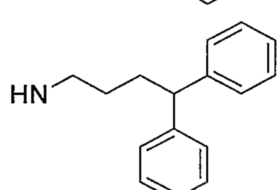	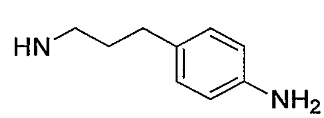
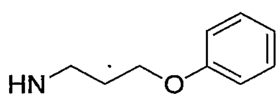	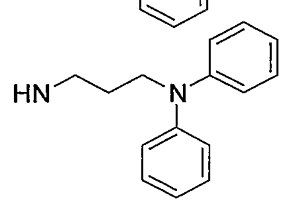	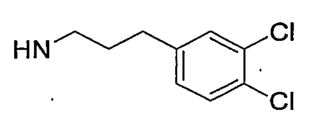
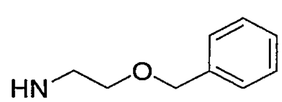		

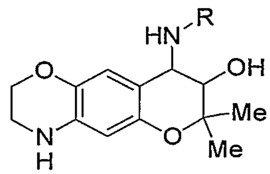

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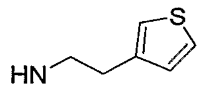	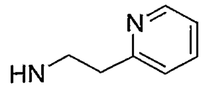	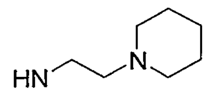	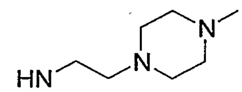
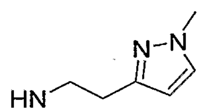	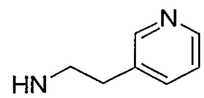	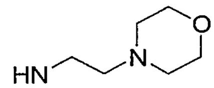	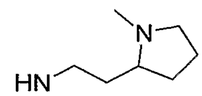
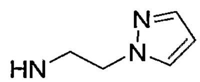	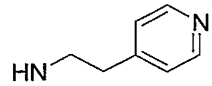	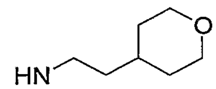	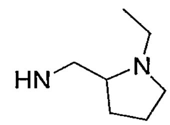
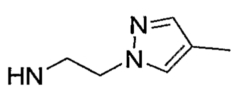	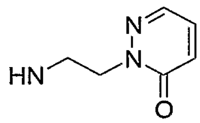	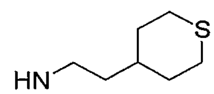	
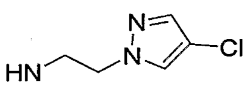	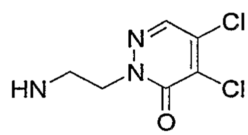	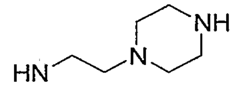	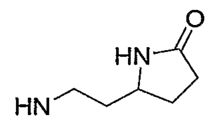
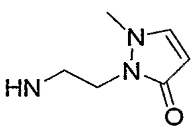	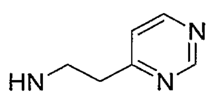	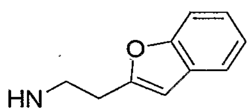	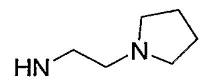
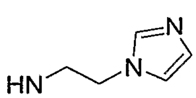	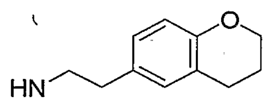	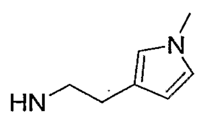	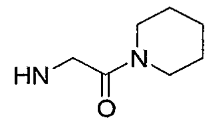
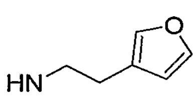	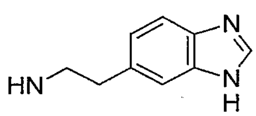	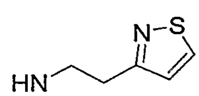	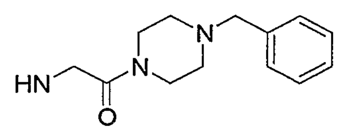
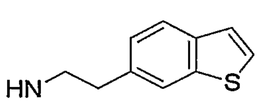	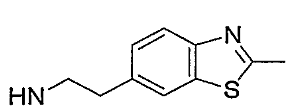	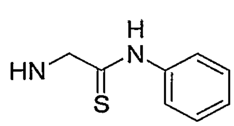	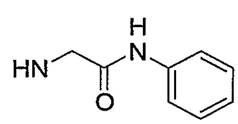

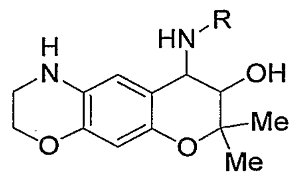

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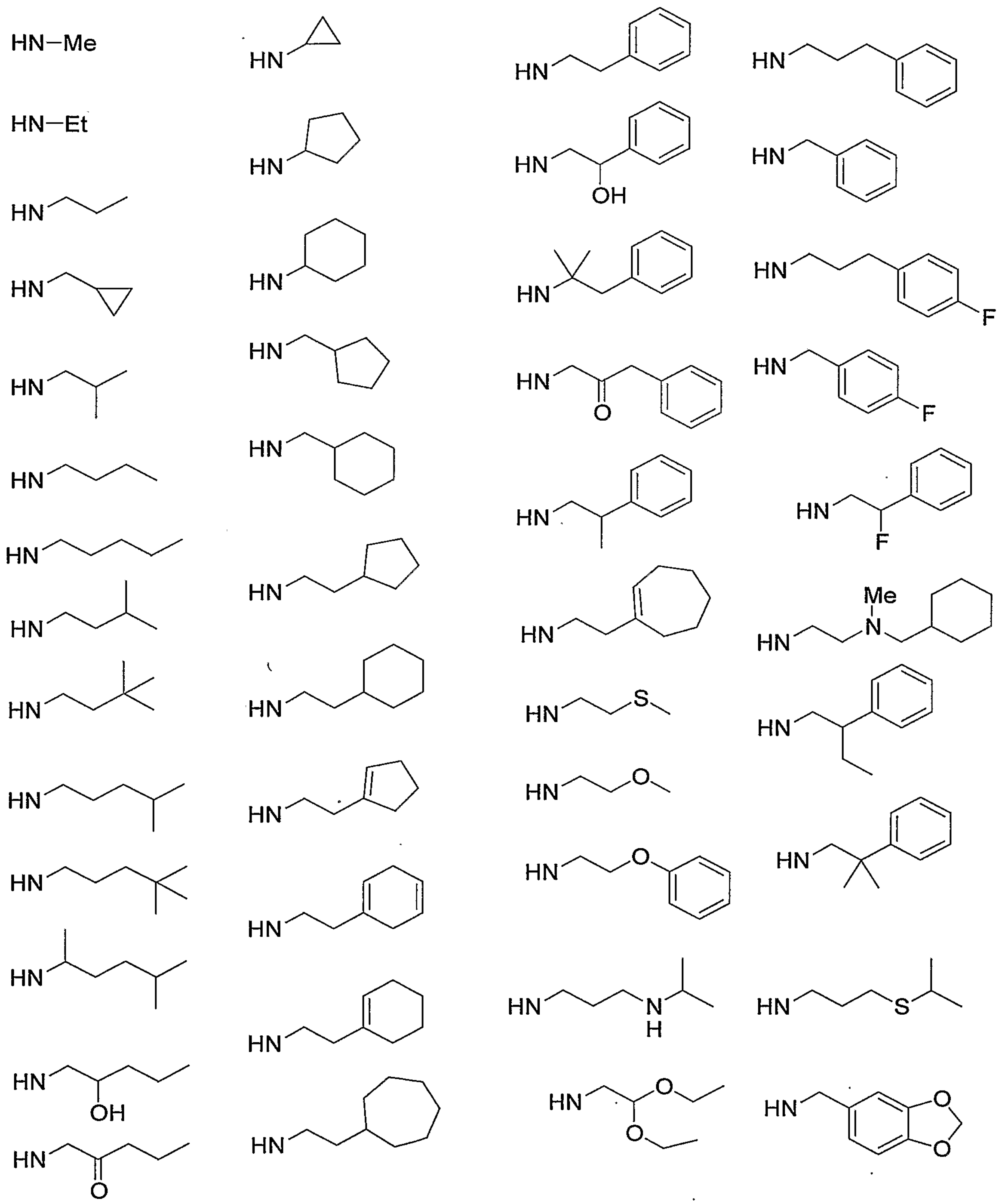

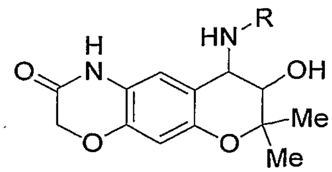

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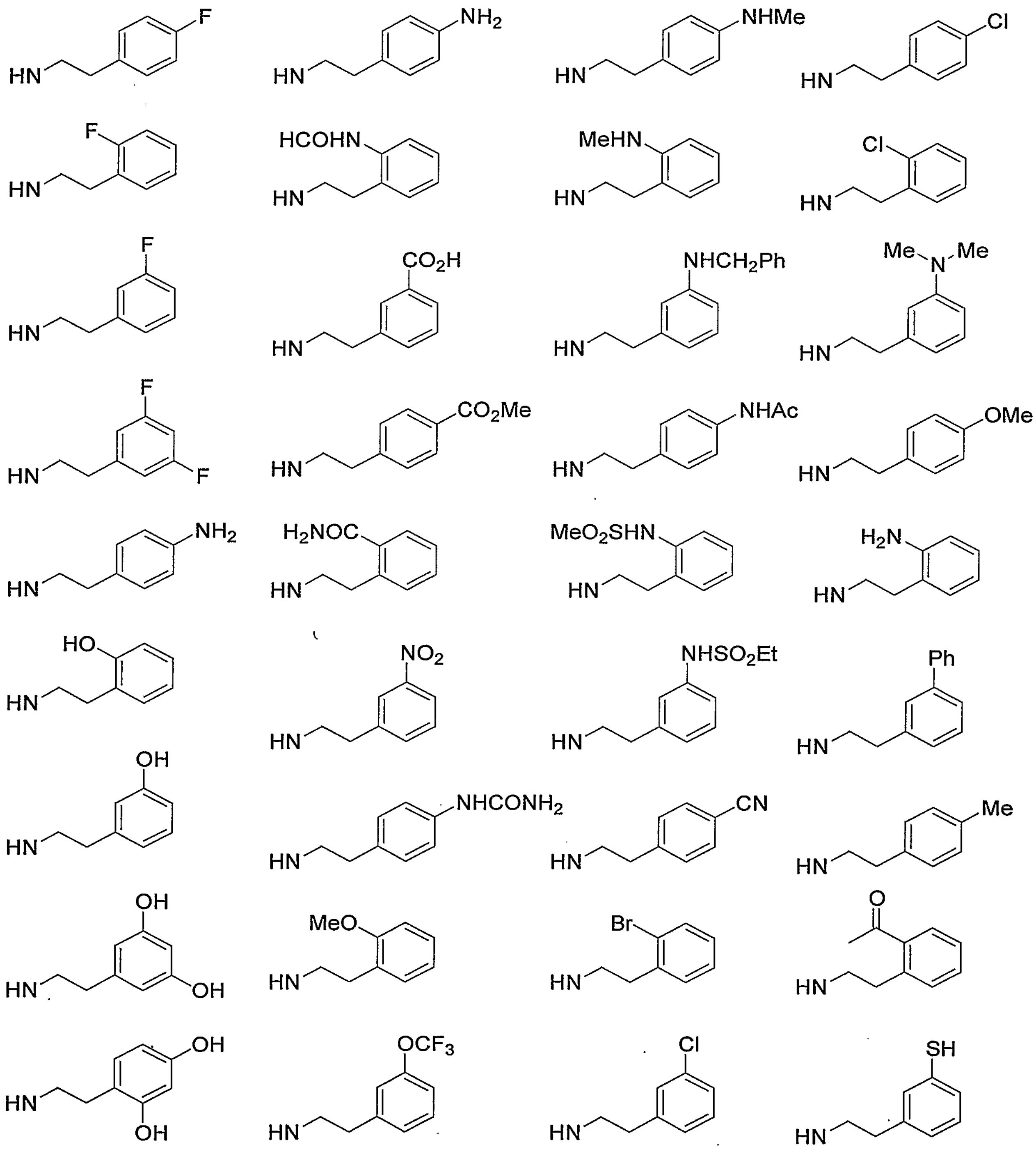

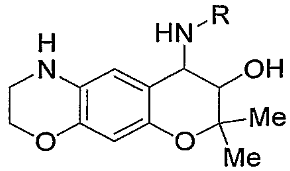

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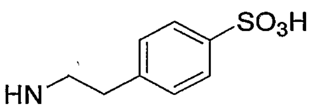
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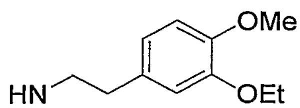
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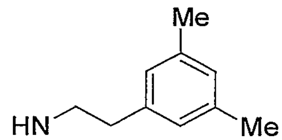
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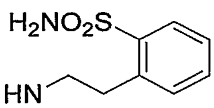
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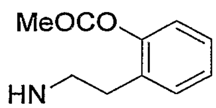
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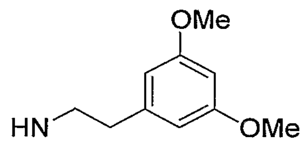
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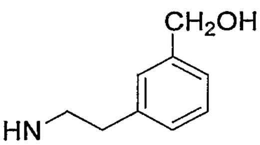
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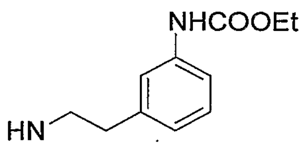
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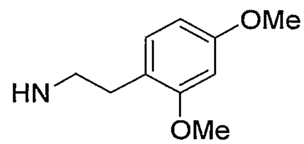
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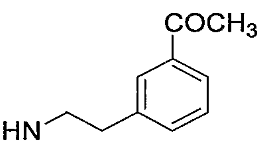
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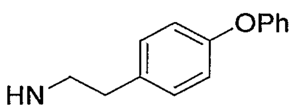
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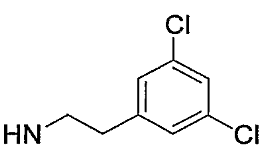
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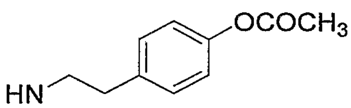
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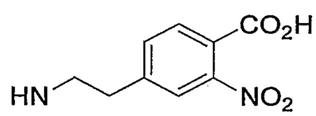
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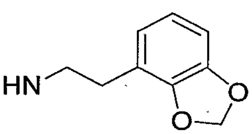
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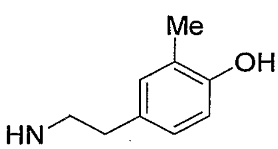
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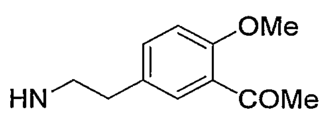
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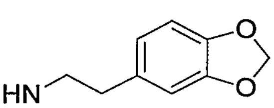
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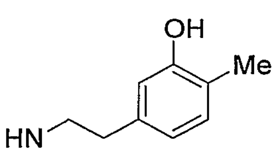
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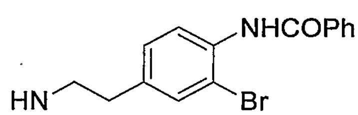
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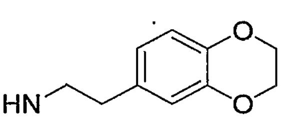
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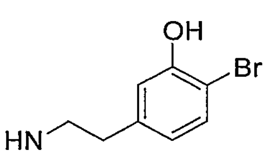
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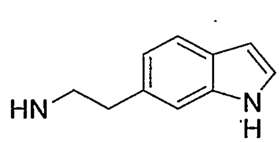
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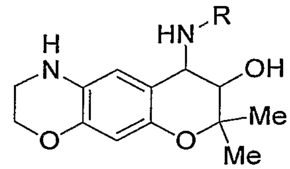

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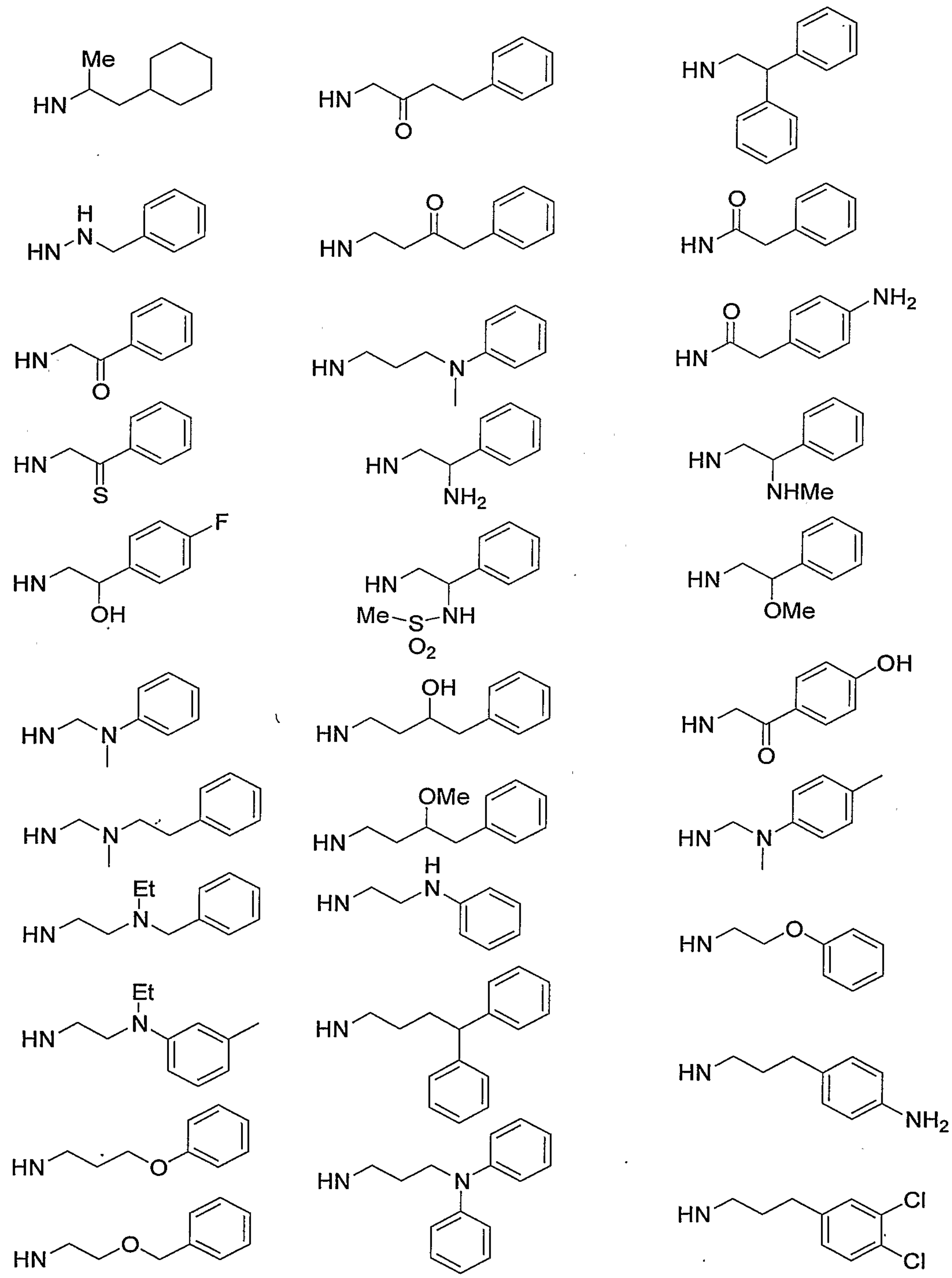

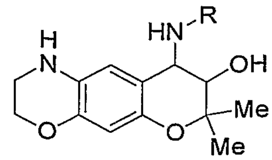

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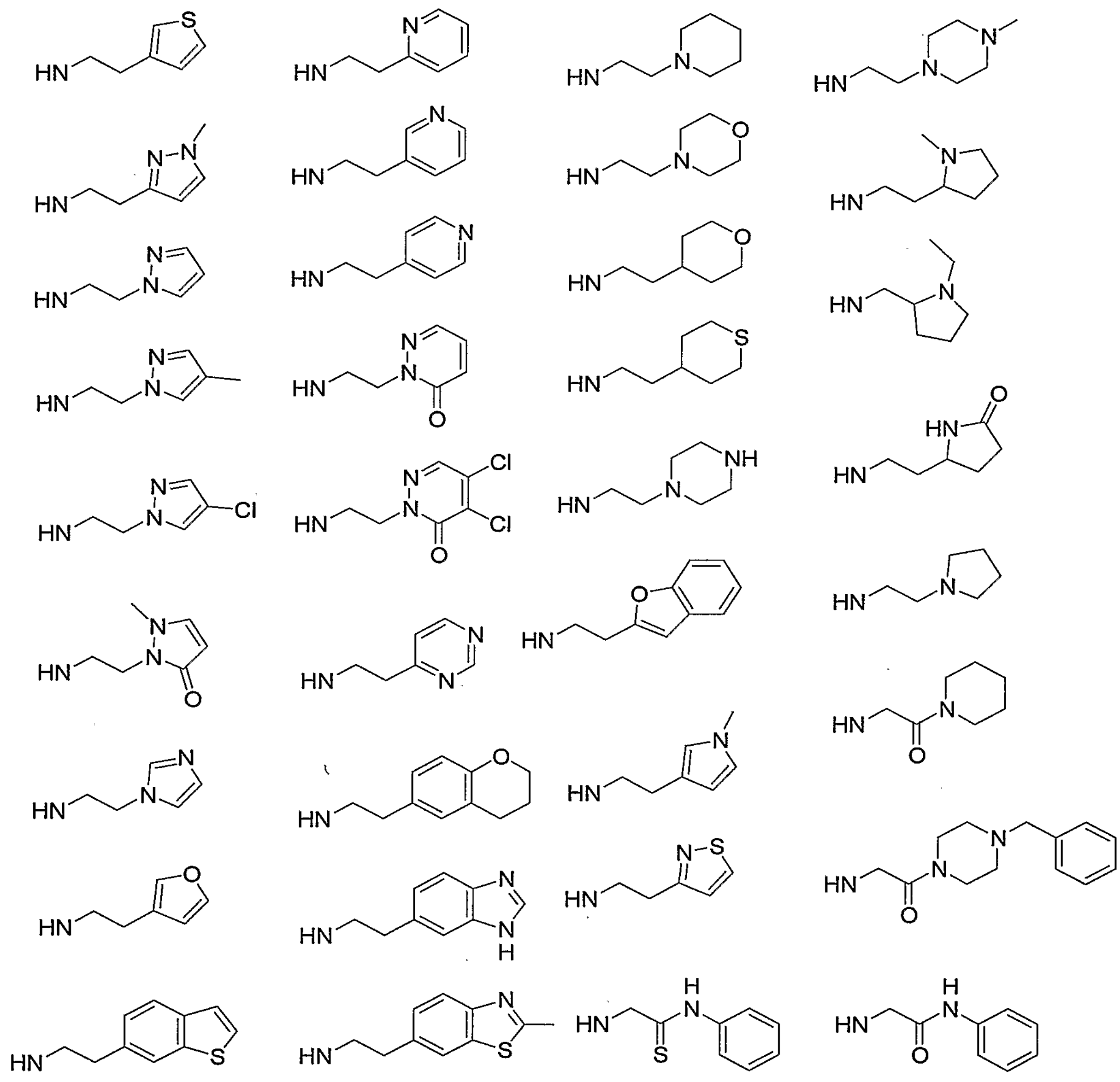

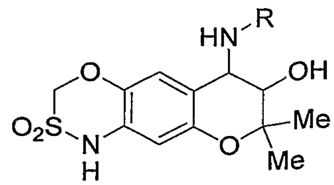

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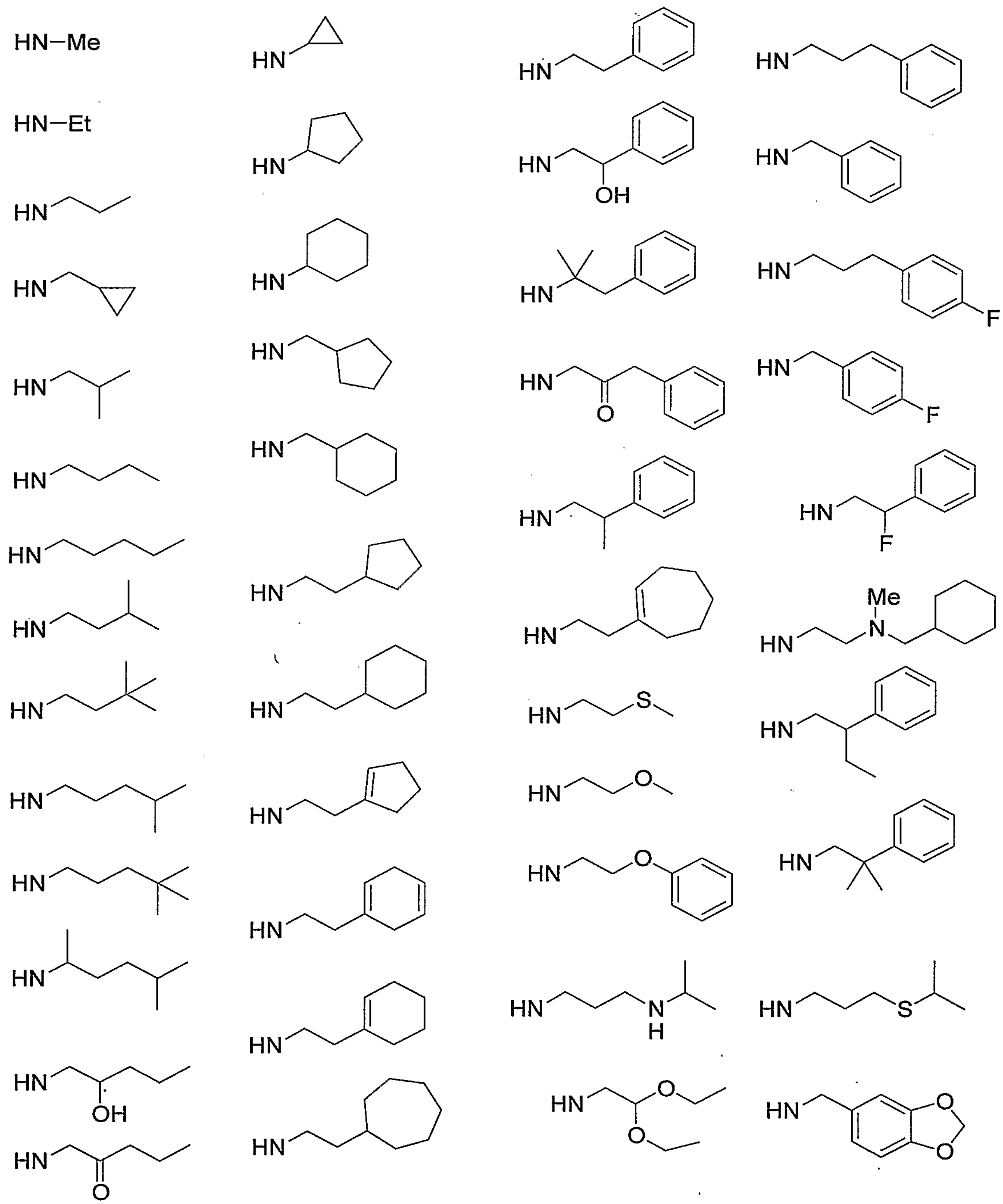

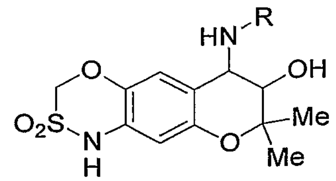

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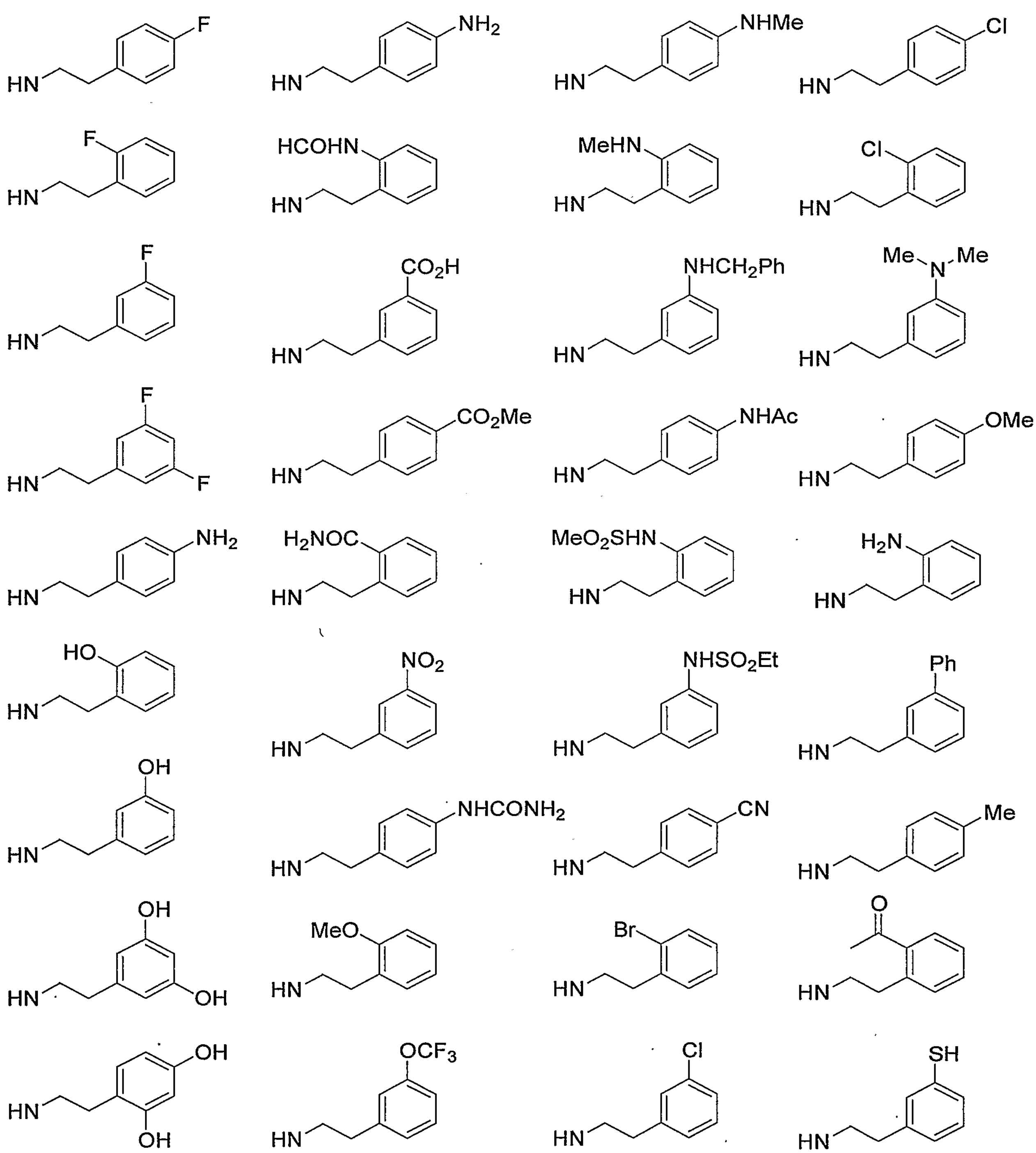

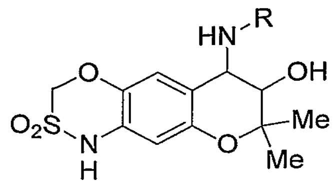

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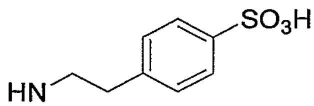	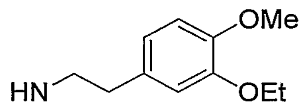	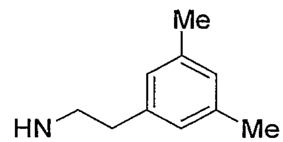
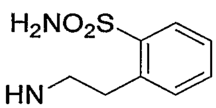	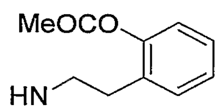	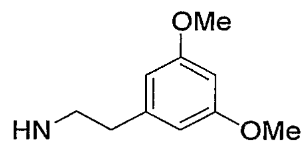
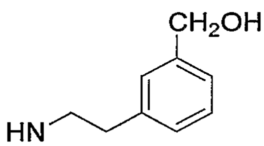	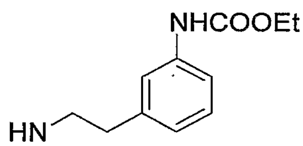	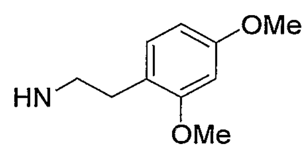
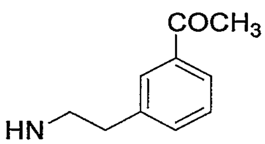	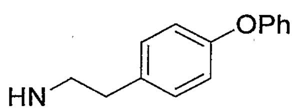	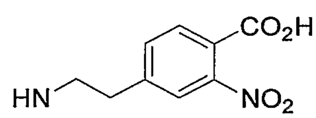
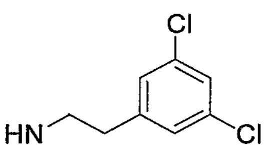	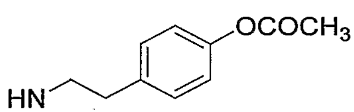	
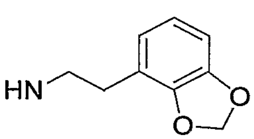	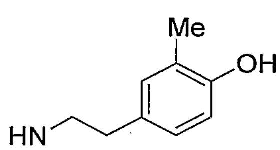	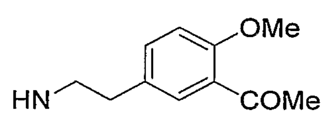
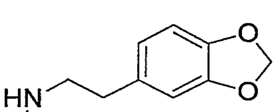	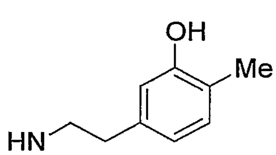	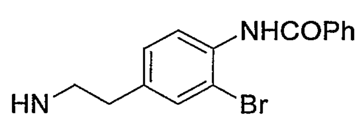
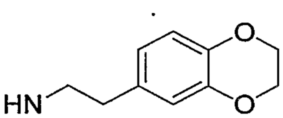	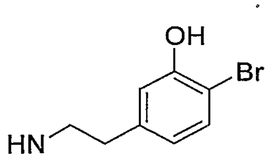	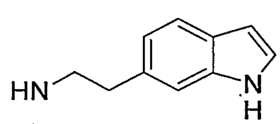

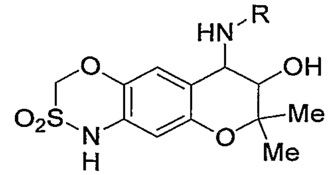

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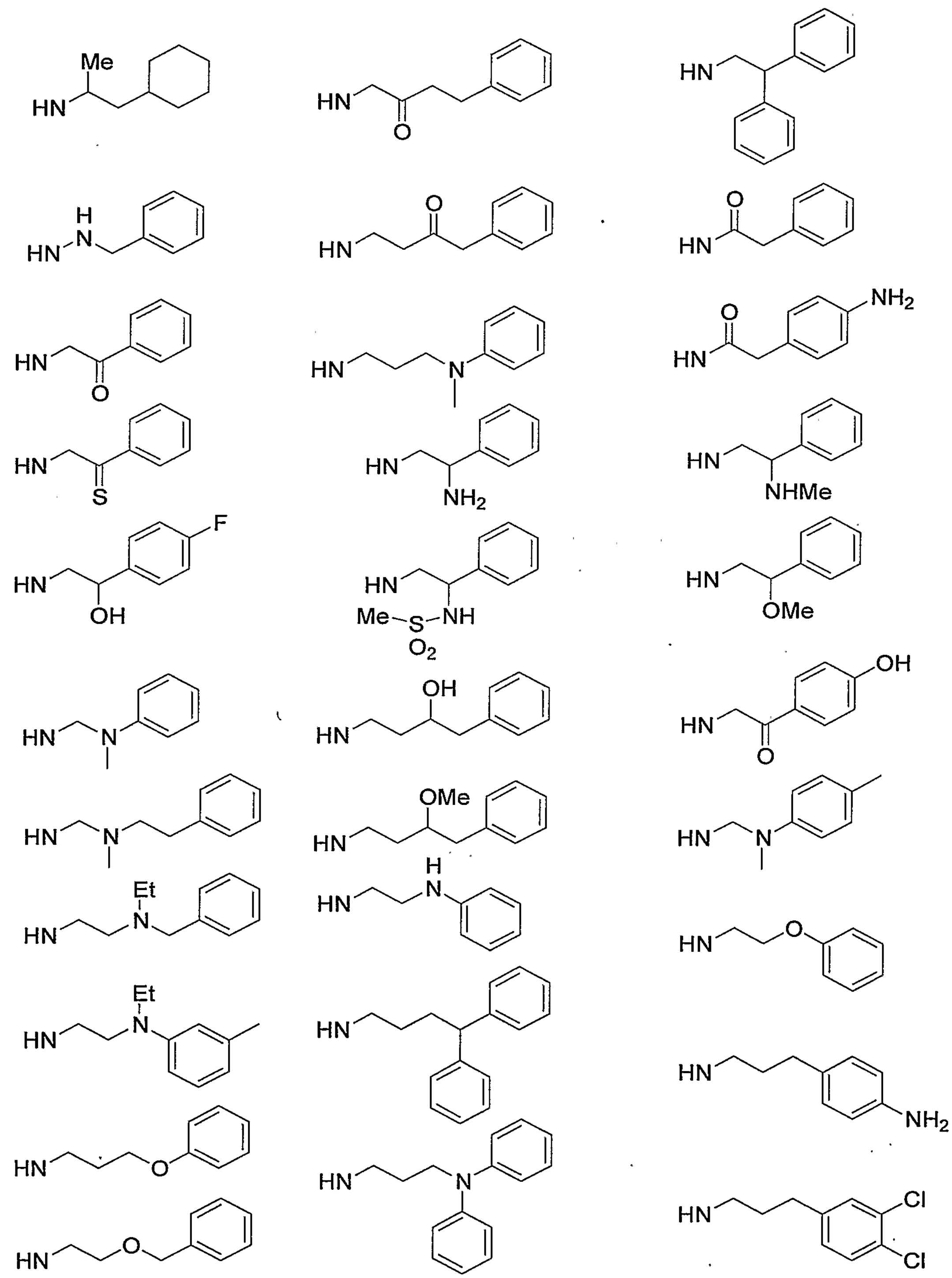

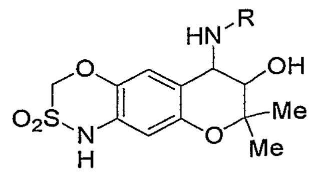

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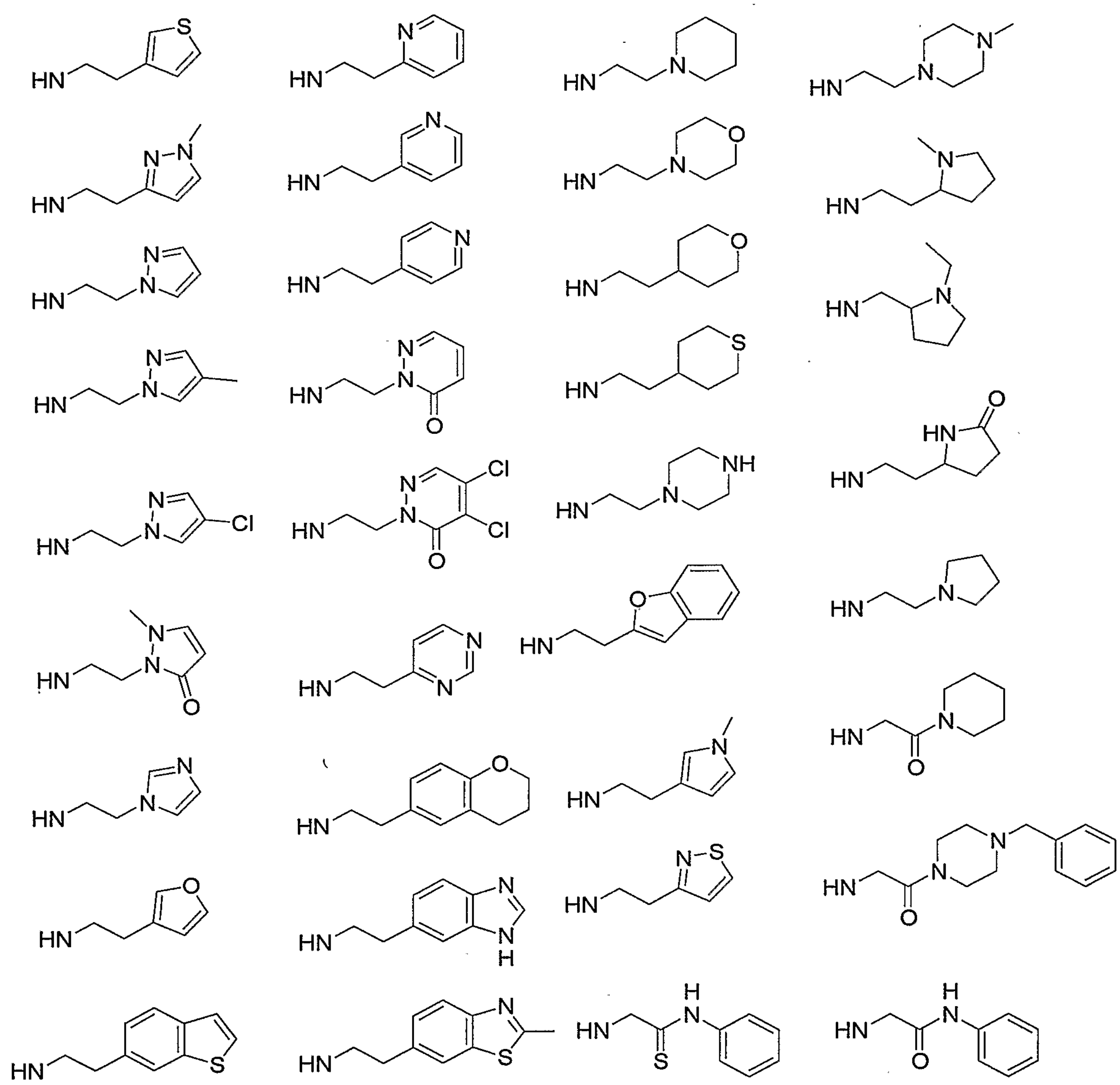

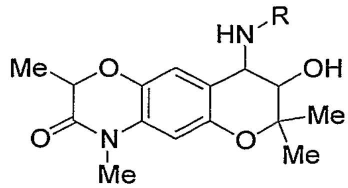

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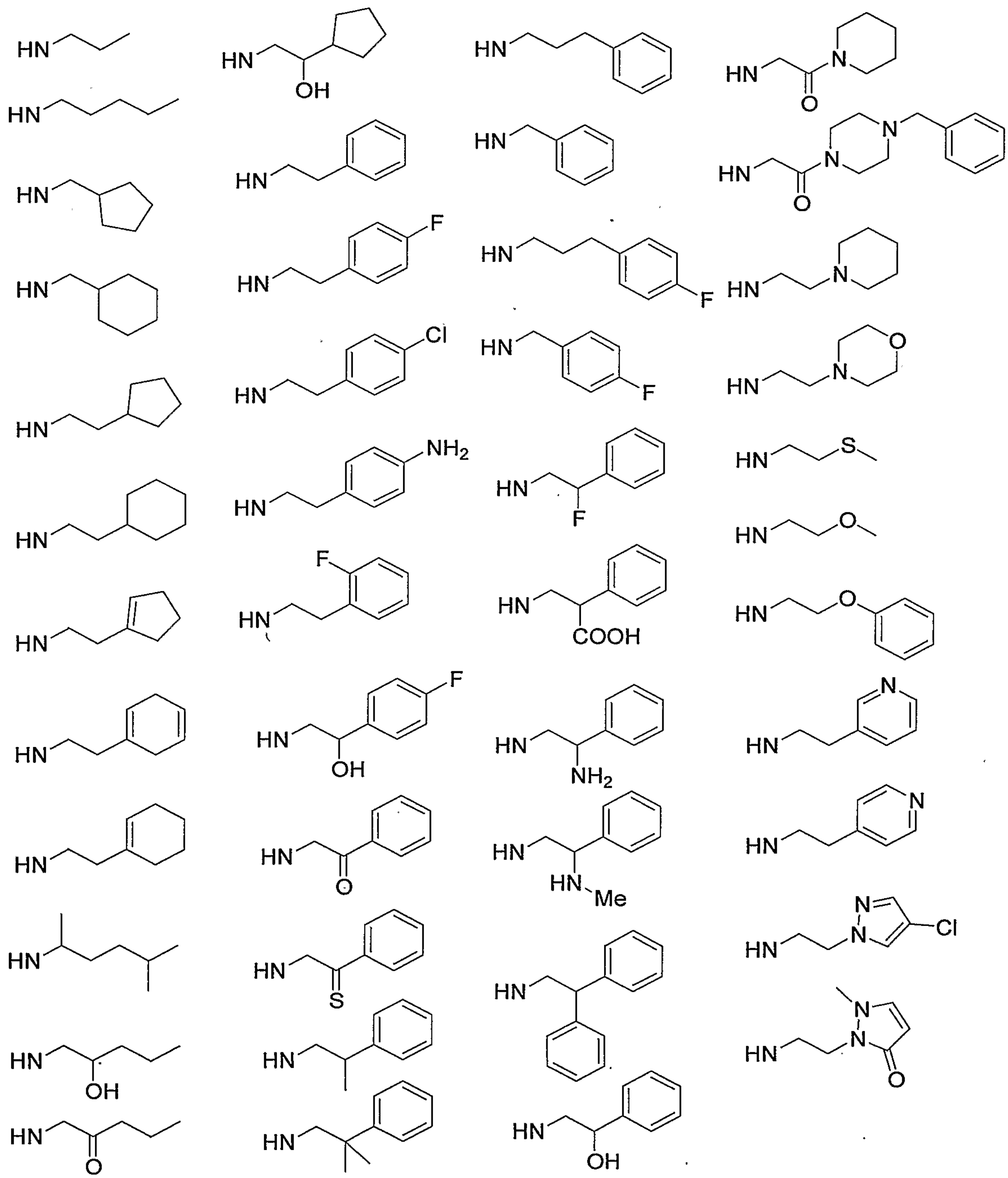

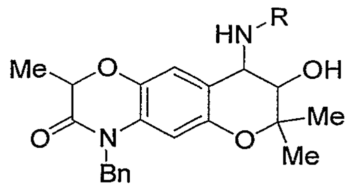

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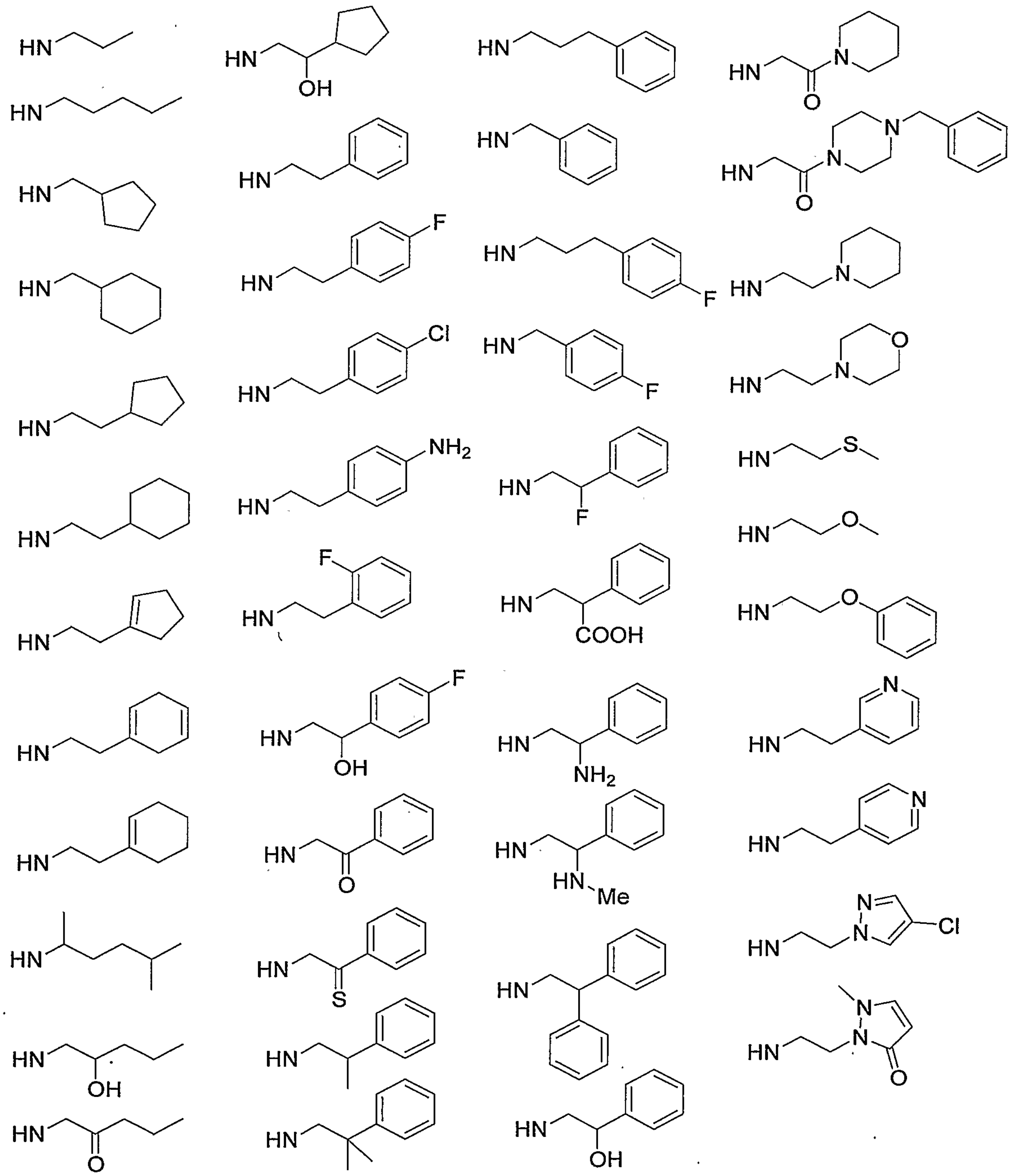

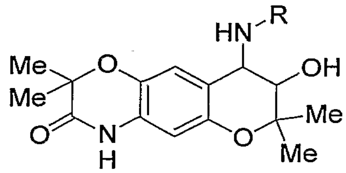

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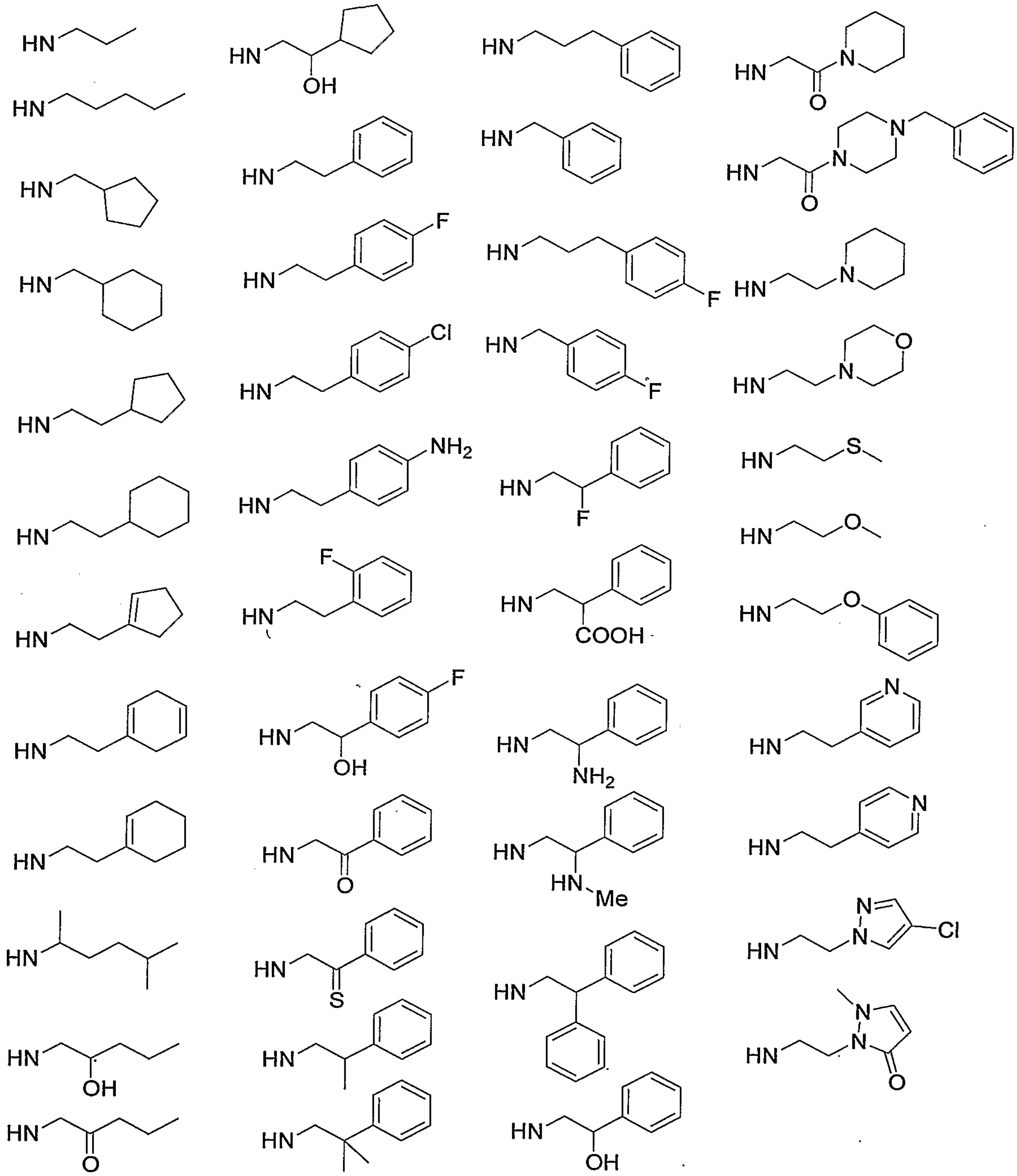

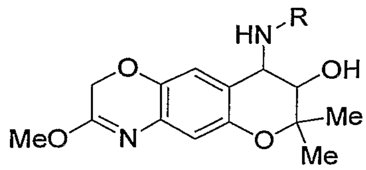

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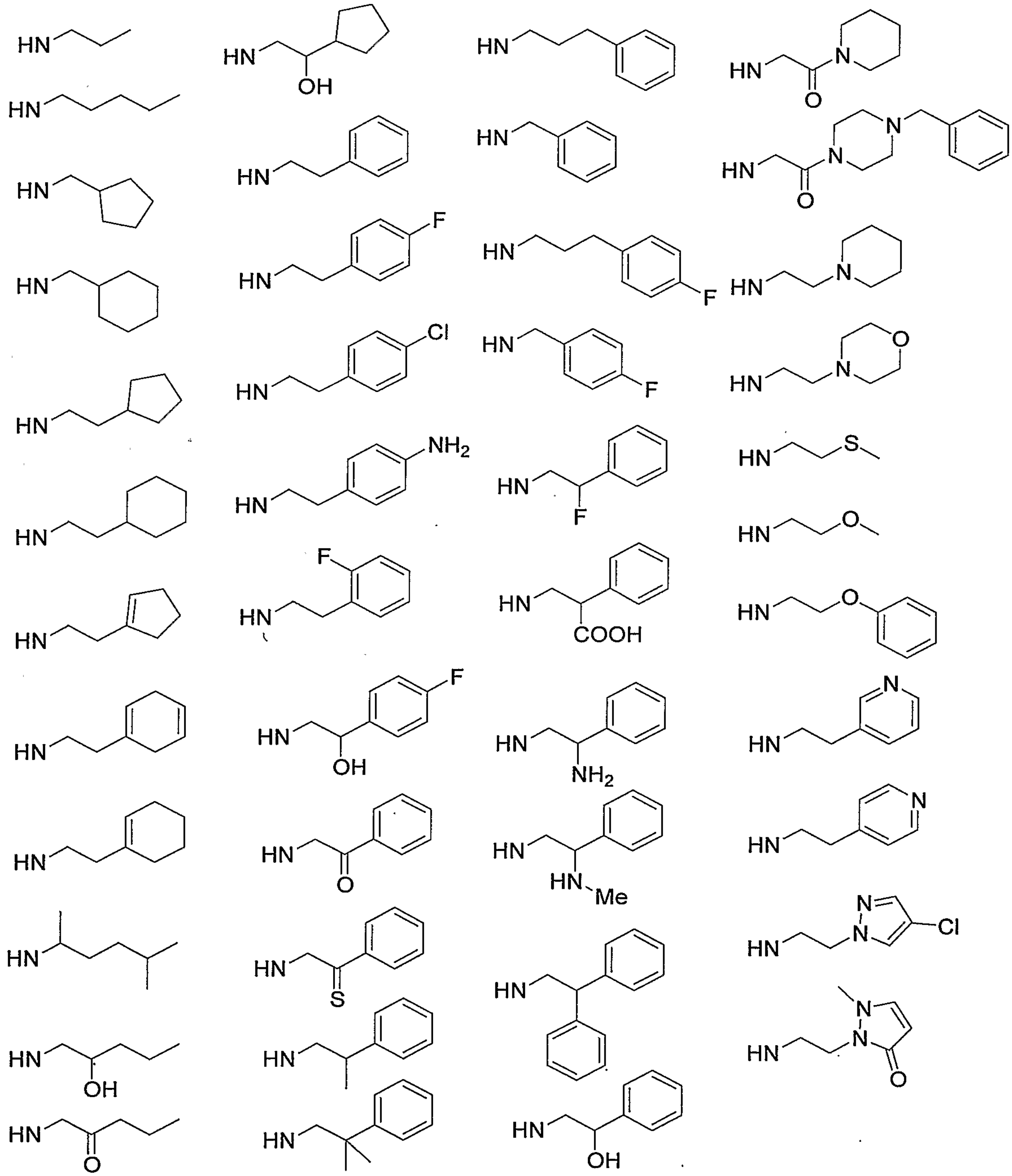

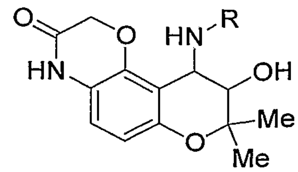

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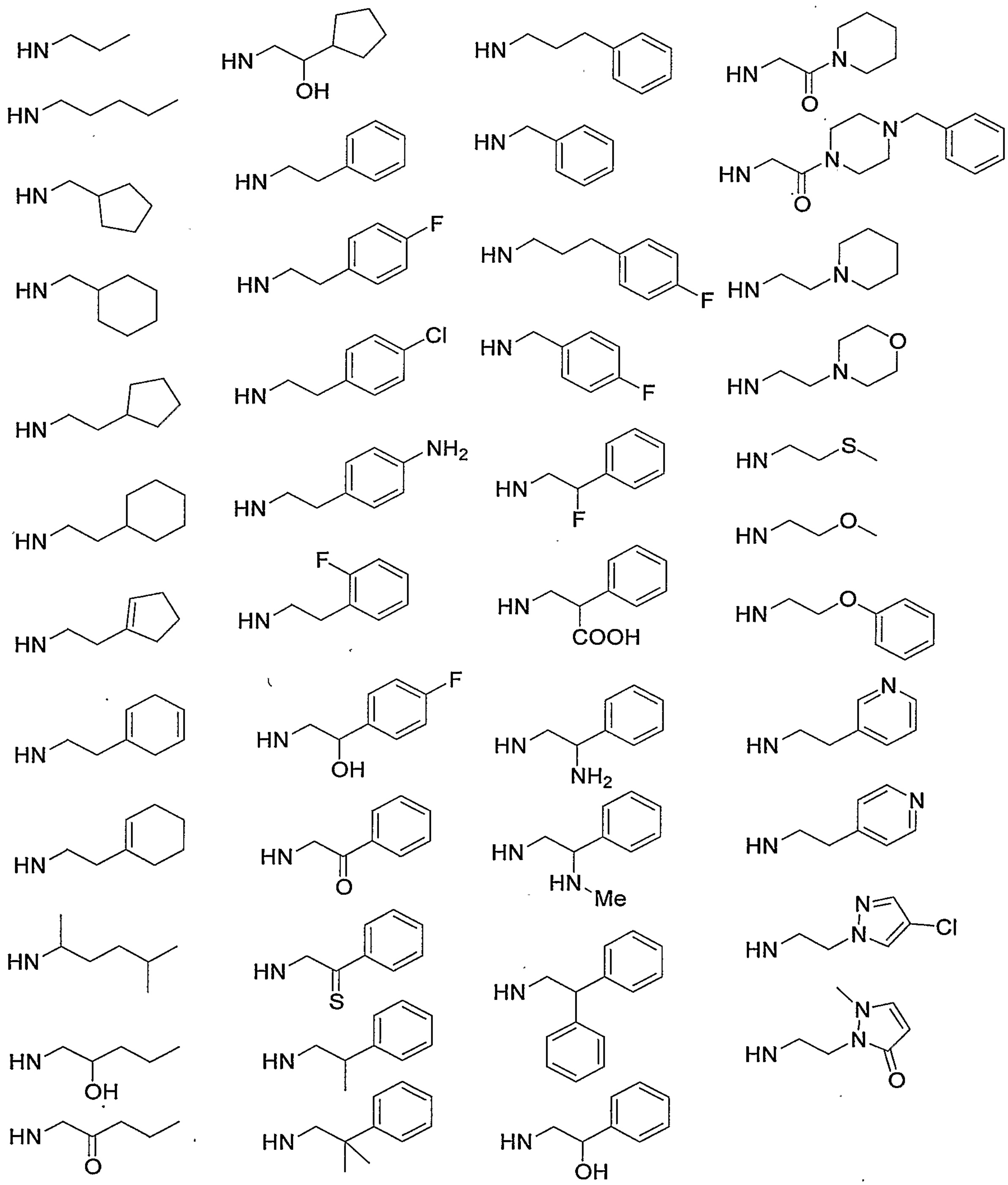

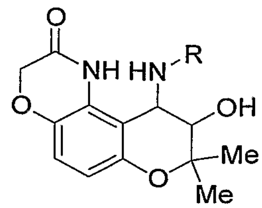

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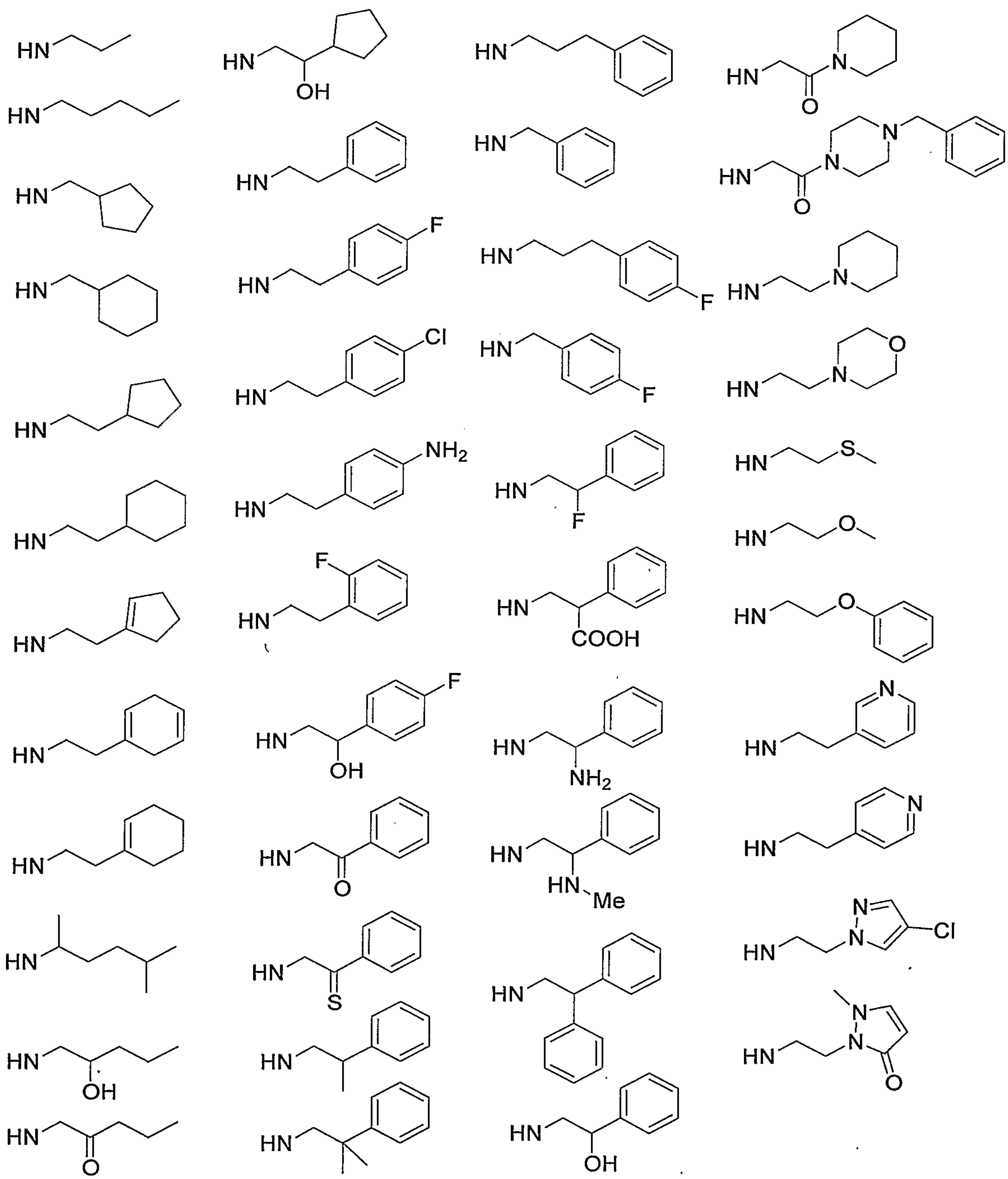

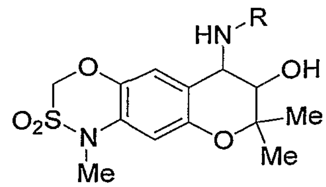

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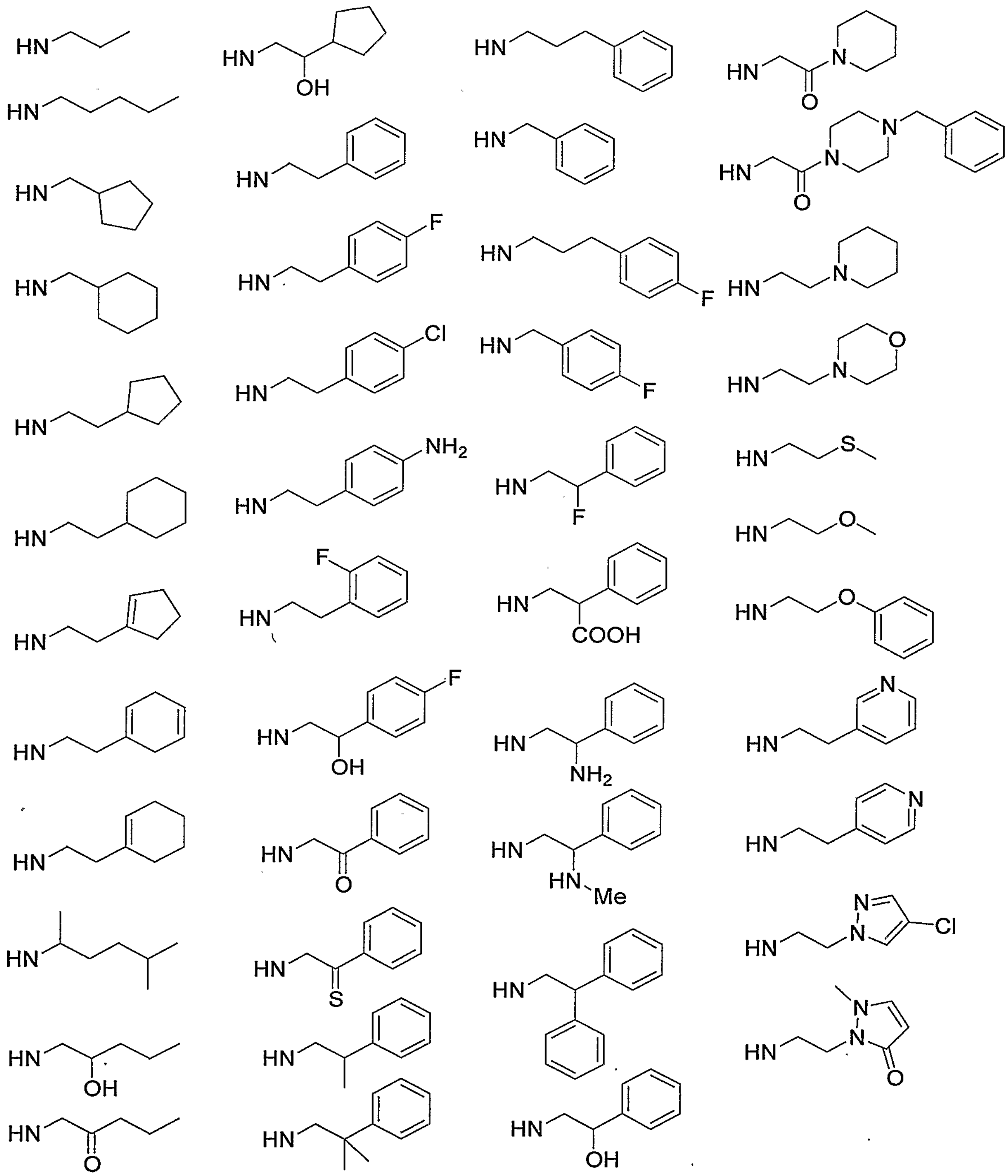

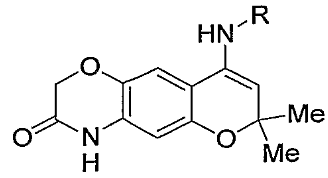

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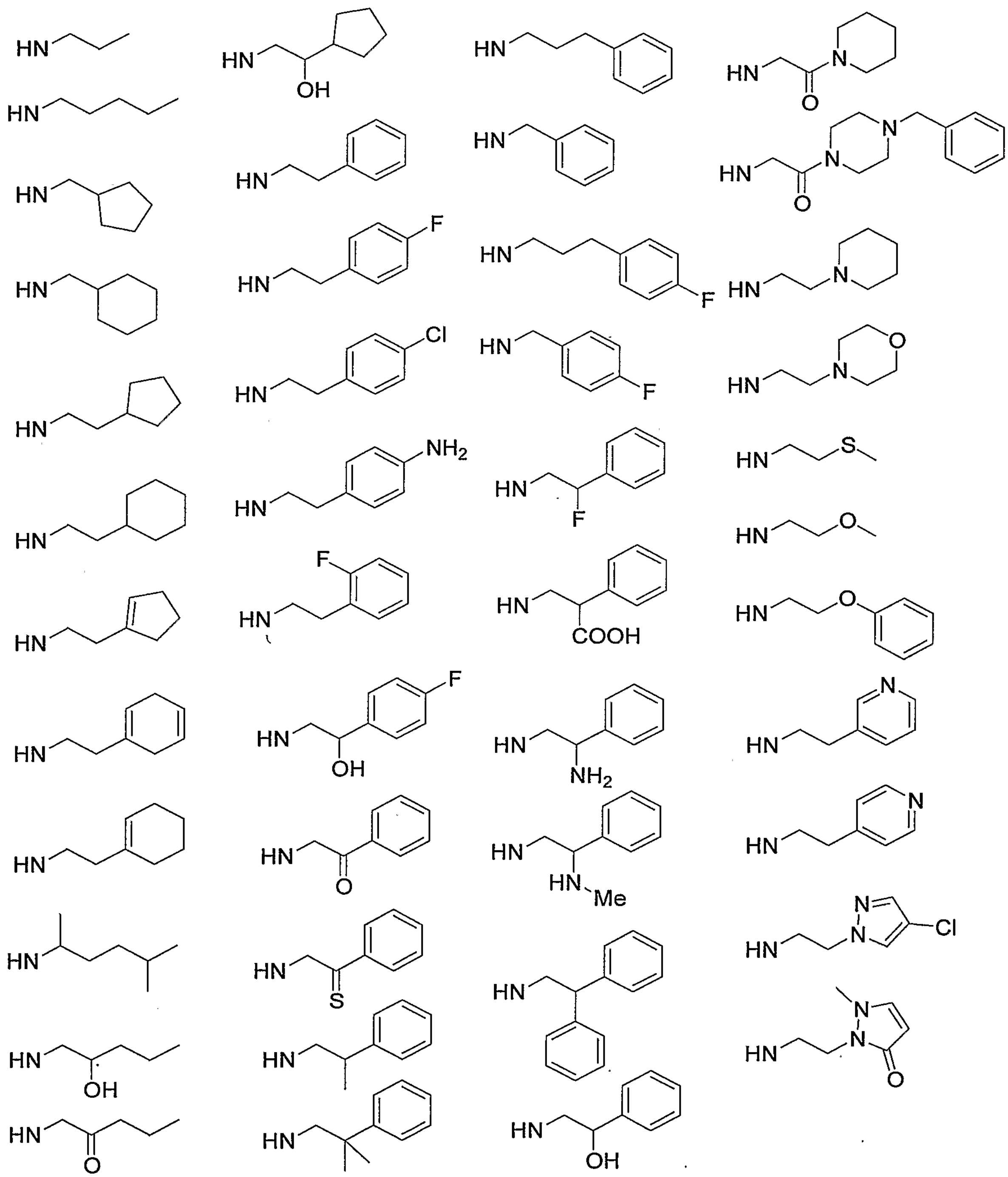
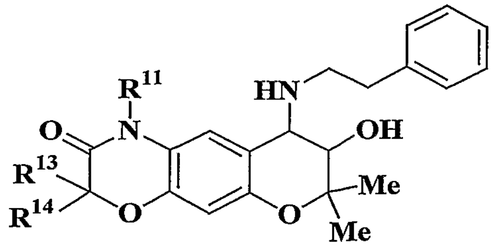
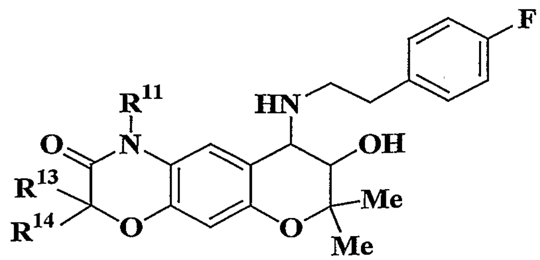




R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

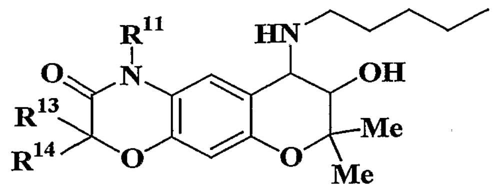
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

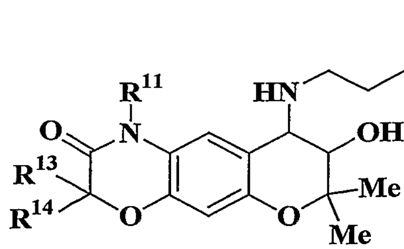
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



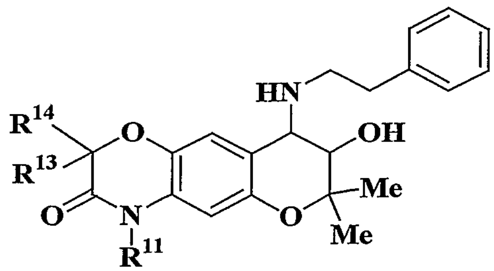
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



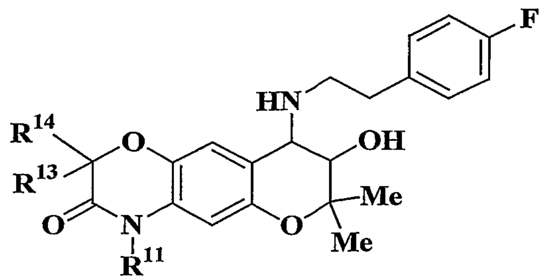
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



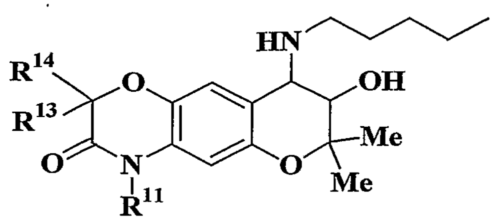
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

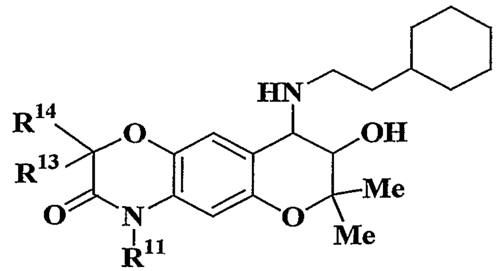
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



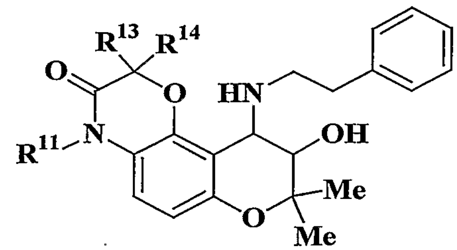
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



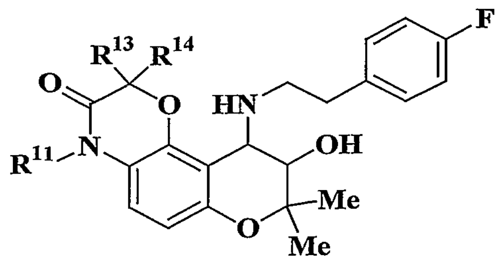
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

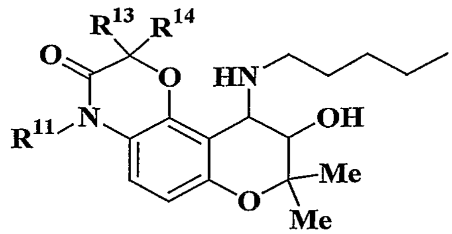
R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



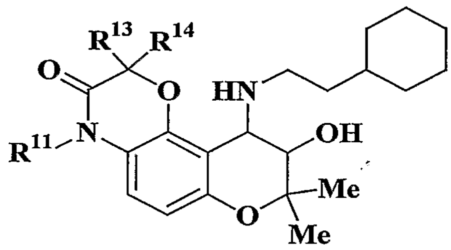
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



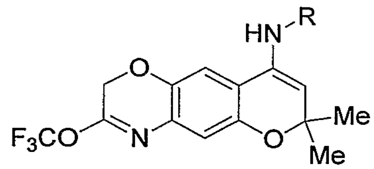
R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}	R^{11}	R^{13}	R^{14}
H	H	Et	H	NO_2	H	H	H	NO_2
H	H	iPr	H	CHO	H	H	H	CHO
H	H	nPr	H	SO_3H	H	H	H	SO_3H
H	H	nBu	H	Cl	H	H	H	Cl
H	H	tBu	H	Br	H	H	H	Br
Me	H	Ph	Me	CH_2OH	H	Me	H	CH_2OH
Me	Et	Ph	Me	CH_2NH_2	H	Me	H	CH_2NH_2
Me	iPr	H	Me	CH_2NHMe	H	Me	H	CH_2NHMe
Me	nPr	H	Me	CH_2Ph	H	Me	H	CH_2Ph
Me	nBu	H	Me	COMe	H	Me	H	COMe
Me	tBu	H	Me	COOH	H	Me	H	COOH
Et	Ph	H	Et	$CONH_2$	H	Et	H	$CONH_2$
Et	H	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	H	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	H	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	Cl	Et	Ph	SO_3H	Et	Ph	Et	H
CH_2OH	Cl	nPr	CH_2OH	SO_2NHMe	nPr	CH_2OH	nPr	H
CH_2OH	Cl	Ph	CH_2OH	OH	Ph	CH_2OH	Ph	H
CH_2OMe	Et	Cl	CH_2OMe	COMe	Cl	CH_2OMe	Cl	Cl
CH_2OMe	nPr	Cl	CH_2OMe	COOH	Cl	CH_2OMe	Cl	Cl
CH_2NH_2	Ph	Cl	CH_2NH_2	$CONH_2$	Cl	CH_2NH_2	Cl	Cl
CH_2NH_2	H	Et	CH_2NH_2	CONHMe	Et	CH_2NH_2	Et	H
CH_2NH_2	H	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	H
CH_2NH_2	H	Ph	CH_2NH_2	NHMs	Ph	CH_2NH_2	Ph	H
CH_2NHMe	Me	Me	CH_2NHMe	NO_2	Me	CH_2NHMe	Me	H
CH_2Ph	Et	Et	CH_2Ph	OH	Et	CH_2Ph	Et	H
CH_2Ph	nPr	nPr	CH_2Ph	COMe	nPr	CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH_2CH_2Ph	Ph	H



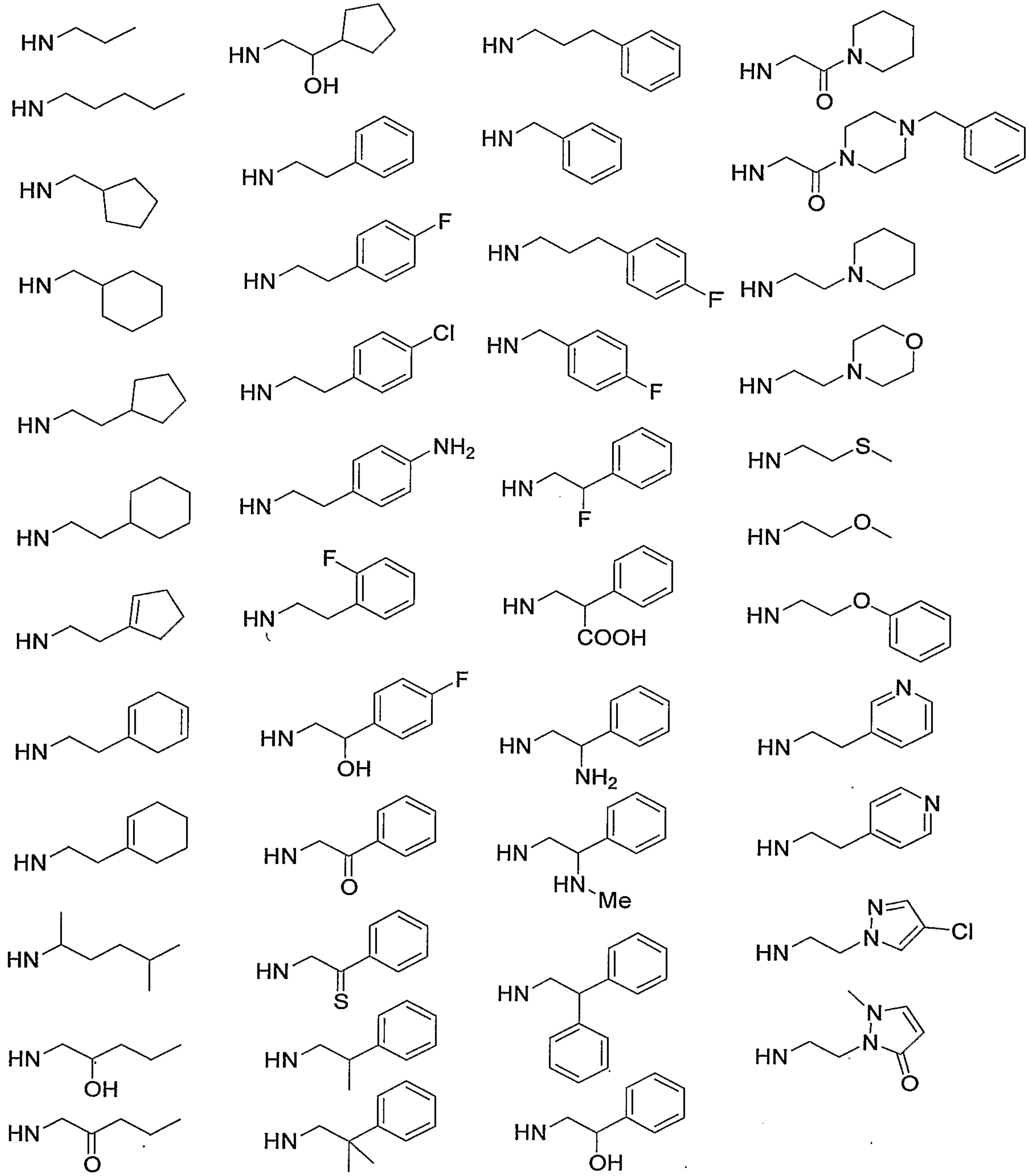
R^{11}	R^{13}	R^{14}
H	H	Et
H	H	iPr
H	H	nPr
H	H	nBu
H	H	tBu
Me	H	Ph
Me	Et	Ph
Me	iPr	H
Me	nPr	H
Me	nBu	H
Me	tBu	H
Et	Ph	H
Et	H	Et
Et	H	iPr
iPr	H	nPr
nPr	H	nBu
nBu	H	tBu
tBu	H	Ph
Ph	Cl	Et
CH_2OH	Cl	nPr
CH_2OH	Cl	Ph
CH_2OMe	Et	Cl
CH_2OMe	nPr	Cl
CH_2NH_2	Ph	Cl
CH_2NH_2	H	Et
CH_2NH_2	H	nPr
CH_2NH_2	H	Ph
CH_2NHMe	Me	Me
CH_2Ph	Et	Et
CH_2Ph	nPr	nPr
CH_2CH_2Ph	Ph	Ph

R^{11}	R^{13}	R^{14}
H	NO_2	H
H	CHO	H
H	SO_3H	H
H	Cl	H
H	Br	H
Me	CH_2OH	H
Me	CH_2NH_2	H
Me	CH_2NHMe	H
Me	CH_2Ph	H
Me	COMe	H
Me	COOH	H
Et	$CONH_2$	H
Et	CONHMe	Et
Et	CONHMs	iPr
iPr	NHMs	nPr
nPr	NHCOMe	nBu
nBu	NO_2	tBu
tBu	CHO	Ph
Ph	SO_3H	Et
CH_2OH	SO_2NHMe	nPr
CH_2OH	OH	Ph
CH_2OMe	COMe	Cl
CH_2OMe	COOH	Cl
CH_2NH_2	$CONH_2$	Cl
CH_2NH_2	CONHMe	Et
CH_2NH_2	CONHMs	nPr
CH_2NH_2	NHMs	Ph
CH_2NHMe	NO_2	Me
CH_2Ph	OH	Et
CH_2Ph	COMe	nPr
CH_2CH_2Ph	COOH	Ph

R^{11}	R^{13}	R^{14}
H	H	NO_2
H	H	CHO
H	H	SO_3H
H	H	Cl
H	H	Br
Me	H	CH_2OH
Me	H	CH_2NH_2
Me	H	CH_2NHMe
Me	H	CH_2Ph
Me	H	COMe
Me	H	COOH
Et	H	$CONH_2$
Et	Et	CONHMe
Et	iPr	CONHMs
iPr	nPr	NHMs
nPr	nBu	NHCOMe
nBu	tBu	NO_2
tBu	Ph	H
Ph	Et	H
CH_2OH	nPr	H
CH_2OH	Ph	H
CH_2OMe	Cl	Cl
CH_2OMe	Cl	Cl
CH_2NH_2	Cl	Cl
CH_2NH_2	Et	H
CH_2NH_2	nPr	H
CH_2NH_2	Ph	H
CH_2NHMe	Me	H
CH_2Ph	Et	H
CH_2Ph	nPr	H
CH_2CH_2Ph	Ph	H



HN—R



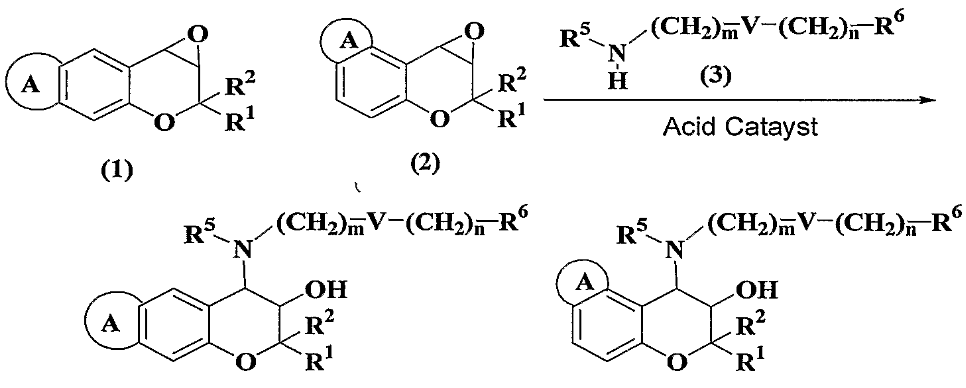
The compound according to the present invention has asymmetric carbon atoms at 3-position and 4-position, thus optical isomers thereof based on the asymmetric carbon atoms are present, and optical active substances can be also used in the application of the present invention, like racemic modifications. Further, cis- and trans-isomer based on configuration at 3-position and 4-position may be included, but trans-isomer is preferred.

Further, when the compounds can form their salts, the pharmaceutically acceptable salts thereof can also be used as active ingredients.

Examples of pharmaceutically acceptable salt are such as hydrochlorides, hydrobromides, sulfates, methanesulfonates, acetates, benzoates, tartrates, phosphates, lactates, maleates, fumarates, malates, gluconates, salicylates and the like.

Preferably, hydrochlorides, maleates and methanesulfonates may be mentioned.

The compound of formula (I-a) or (II-a) that is the compound of formula (I) or (II) wherein R^4 is hydrogen atom and R^3 is hydroxy group can be obtained by reacting the compound of formula (1) or (2) with the compound of formula (3) in an inert solvent as shown in the scheme below.



(1) (2) (I-a) (II-a)

As the solvents used in the reaction of the compound of formula (1) or (2) with the compound of formula (3), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran and dioxane; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type

solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents, nitrile type solvents and alcohol type solvents may be mentioned.

The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 100°C.

The molar ratio of the reaction materials is within the range of 0.5-4.0, preferably 1.0-2.0, for compound (3)/compound (1) or (2).

Acid catalysts may be used in the reaction.

The acid catalysts used include inorganic acids exemplified by hydrochloric acid and sulfuric acid, Lewis acids exemplified by aluminum chloride, titanium tetrachloride, boron trifluoride diethylether complex, perchloric acid, lithium perchlorate, lithium bromide and ytterbium trifluoromethanesulfonate.

Preferable acid catalysts are lithium bromide and lithium perchlorate.

The synthesis of optically active compounds in the compounds of formula (I) or (II) is accomplished by use of a method for optical resolution of racemate (Japanese Patent Laid-open No. Hei 3-141286, US Patent No. 5097037 and EP Patent No. 409165).

In addition, the synthesis of the compound of formula (1) or (2) is accomplished by use of the following synthetic process:

- General synthetic process of benzopyran ring

The benzopyran ring can be synthesized according to known methods (methods described in J. M. Evans et al., J. Med. Chem. 1984, 27, 1127; J. Med. Chem. 1986, 29, 2194; J. T. North et al., J. Org. Chem. 1995, 60, 3397; as well as Japanese Patent Laid-open Nos. Sho 56-57785, Sho 56-57786, Sho 58-188880, Hei 2-141, Hei 10-87650 and Hei 11-209366 and the like.);

- Indole or oxyindole

T. Sakamoto, et al., Heterocycles, 1986, *24*, 31,

M. Belley, et.al., Synthesis, 2001, 222,

A.D. Cross, et al., J. Chem. Soc., 1961, 2714;

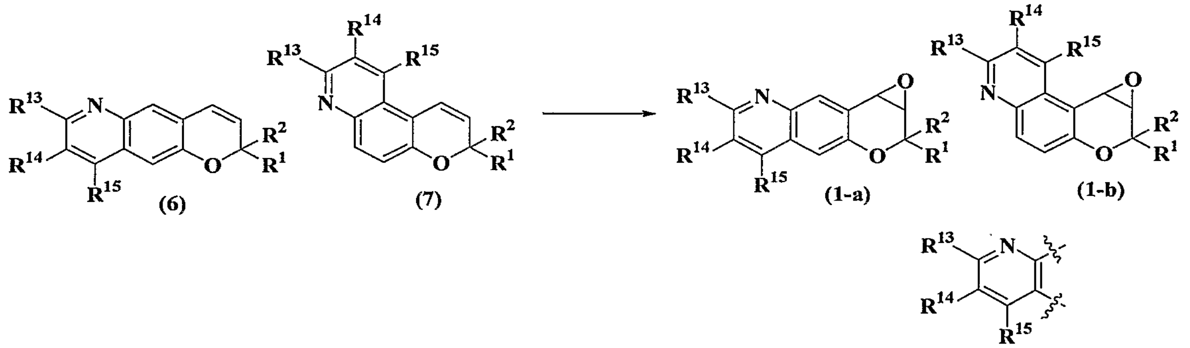
- Imidazolinone

J. Kitteringham, et.al., Synthetic Commun., 2000, *30*, 1937;

- Quinoline

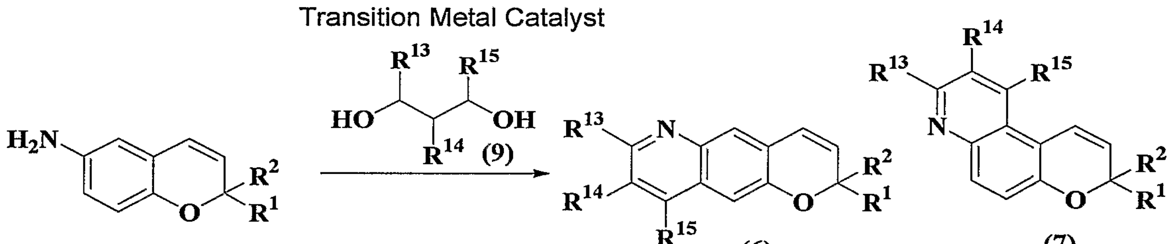
S. Imor, et al., Synthetic Commun., 1996, *26*, 2197,
Y. Kitahara, et al., Tetrahedron, 1997, *53*, 6001,
A.G. Osborne, et al., J. Chem. Soc. Perkin Trans. 1, 1993, 181,
R. T. Shuman, et al., J. Org. Chem., 1990, *55*, 738,
T. Sakamoto, et al., Chem. Pharm. Bull., 1981, *29*, 2485,
Y. Tsuji, et al., J. Org. Chem., 1987,*52*, 1673,
Z. Song, et al., J. Heterocyclic Chem., 1993, *30*, 17;
- Quinolinone
M.R. Sabol, et al., Synthetic Commun., 2000, *30*, 427,
Z-Y. Yang, et al., Tetrahedron Lett., 1999, *40*, 4505,
H-B Sun, et al., Synthesis, 1997, 1249,
A. Guiotto, et al., J. Heterocyclic Chem. 1989, *26*, 917,
K. Konno, et al., Heterocycles 1986, *24*, 2169,
E. Fernandez, et al., Synthesis 1995, 1362;
- Benzothiazole or triazole
N.B.Ambati, et al., Synthetic Commun., 1997, *27*, 1487,
D.E. Burton., et al., J. Chem. Soc (C). 1968, 1268;
- Quinoxaline or quinoxalinone
J.H. Liu, et al., J. Org. Chem., 2000, *65*, 3395,
J.J.Li, et al., Tetrahedron Lett., 1999, *40*, 4507,
Y.Ahmed, et al., Bull. Chem. Soc. Jpn.,1987, *60*, 1145;
- Benzoaxadinone
G.H.Jones, et al., J. Med. Chem., 1987, *30*, 295,
J.L. Wright, et al., J. Med. Chem., 2000, *43*, 3408,
M.Kluge, et al., J. Heterocyclic Chem., 1995, *32*, 395.

The compound of formula (1-a) or (2-a) that is the compound of formula (I) or (II) wherein A is the group of formula (5), R^4 is hydrogen atom and R^3 is hydroxy group can be obtained from the compound of formula (6) or (7) according to known methods (methods described in J. M. Evans et al., J. Med. Chem. 1984, 27, 1127; J. Med. Chem. 1986, 29, 2194; J. T. North et al., J. Org. Chem. 1995, 60, 3397; as well as Japanese Patent Laid-open Nos. Sho 56-57785, Sho 56-57786, Sho 58-188880, Hei 2-141, Hei 10-87650 and Hei 11-209366 and the like).



(6) (7) (1-a) (1-b) (5)

The compound of formula (6) or (7) can be obtained by reacting compound (8) with compound (9) (see, Y. Tsuji et al., J. Org. Chem., 1987, 52, 1673).



(8) (9) (6) (7)

As the solvents used in the reaction of the compound of formula (8) with the compound of formula (9), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran, dioxane and diethylene glycol dimethyl ether ; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents, nitrile type solvents and alcohol type solvents may be mentioned.

The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 200°C.

The molar ratio of the reaction materials is within the range of 0.1-4.0, preferably 0.5-2.0, for compound (8)/compound (9).

Transition metal catalysts and ligands may be used in the reaction.

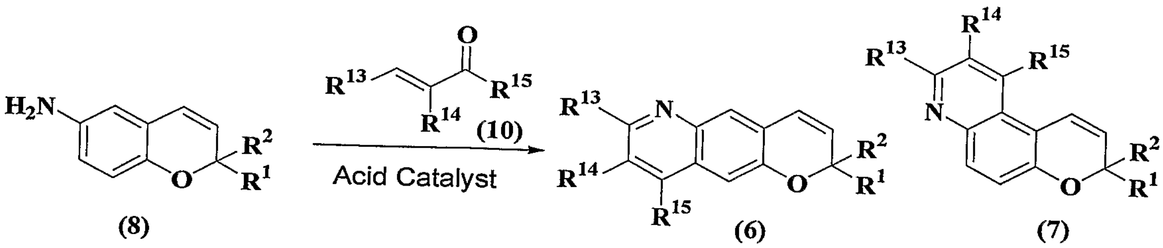
The transition metal catalysts used include ruthenium chloride, dichlorotris(triphenylphosphine)ruthenium, dibromotris(triphenylphosphine)ruthenium, dihydridetetrakis(triphenylphosphine)ruthenium, (η4-cyclooctadiene)(η6-cyclooctatriene)ruthenium, dichlorotricarbonyl ruthenium dimer, dodecacarbonyl triruthenuim, (η5-pentamethylcyclopentadienyl)chloro(η4-cyclooctatriene)ruthenium, palladium acetate, palladium chloride, dichlorobis(triphenylphosphine)palladium, tetrakistriphenylphosphine palladium, bis(dibenzylideneacetone)palladium, rhodium chloride, chlorotris(triphenylphosphine)rhodium, hydridecarbonyltristriphenylphosphine rhodium, hydridetris(triphenylphosphine)rhodium, di-μ-chlorotetracarbonyl dirhodium, chlorocarbonylbis(triphenylphosphine)iridium, (η5-pentamethylcyclopentadienyl)dichloroiridium dimer, nickeltetrakistriphenylphosphine, dicobaltoctacarbonyl, (η5-cycloopentadienyl)dicarbonylcobalt, and the like.

Preferably, ruthenium chloride may be mentioned.

The ligands include monodentate phosphine ligands exemplified by trimethylphosphine, triethylphosphine, tri-*n*-propylphosphine, tri-*i*-propylphosphine, tri-*n*-butylphosphine, tri-*t*-butylphosphine, tricyclohexylphosphine, triphenylphosphine and tri(*o*-tolyl)phosphine, bidentate phosphine ligands exemplified by 1,2-bisdiphenylphosphinoethane, 1,3-bisdiphenylphosphinopropane, 1,4-bisdiphenylphosphinobutane and1,2-diethylphosphinoethane, phosphite ligands exemplified by triethylphosphite, tributylphosphite, triphenylphosphite and tri(*o*-tolyl)phosphite.

Preferably, triphenylphosphine, tri-*n*-butylphosphine and tri-*t*-butylphosphine.

The compound of formula (6) or (7) can be also obtained by reacting compound (8) with compound (10) in the presence of an acid catalyst (see, Y. Kitahara et al., Tetrahedron Lett., 1997, 53, 6001, Z. Song et al., J. Heterocyclic Chem., 1993, 30, 17).



As the solvents used in the reaction of the compound of formula (8) with the compound of formula (10), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran, dioxane and diethylene glycol dimethyl ether; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; organic acid type solvents exemplified by acetic acid and trifluoroacetic acid; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents, nitrile type solvents, alcohol type solvents and organic acid type solvents may be mentioned.

The acid catalysts used include inorganic acids exemplified by hydrochloric acid, sulfuric acid, nitric acid and phosphoric acid, organic sulfonic acids exemplified by methane sulfonic acid and paratoluene sulfonic acid, Lewis acids exemplified by aluminum chloride, titanium tetrachloride, boron trifluoride diethylether complex, perchloric acid, zinc chloride, zinc bromide, zinc iodide, iron(III) chloride, iron(II) chloride. copper(I) chloride and copper(II) chloride. Preferably, hydrochloric acid and zinc chloride may be mentioned.

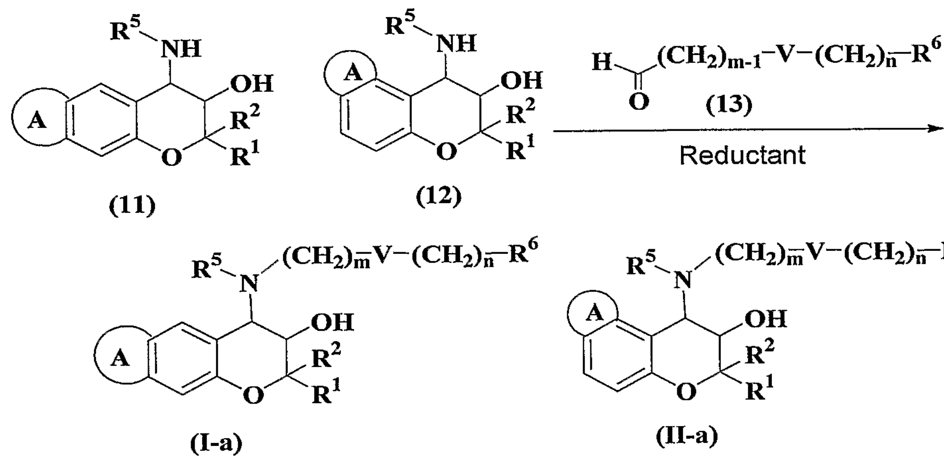
The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 200°C.

The molar ratio of the reaction materials is within the range of 1-10, preferably 1-3, for compound (10)/compound (8).

Furthermore, syntheses of optically active compounds in the compounds of of formula (1) or (2) can be attained by utilizing asymmetric synthetic methods (PCT

Japanese Translation Patent Publication No. Hei 5-507645, Japanese Patent Laid-open Nos. Hei 5-301878 and Hei 7-285983, European Patent Laid-open No.535377 and U.S. Patent No. 5420314).

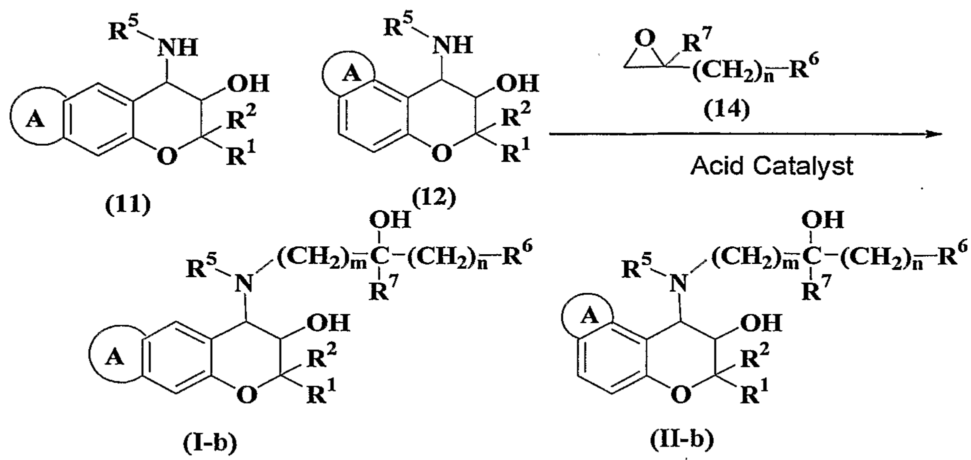
The compound of formula (I-a) or (II-a) that is the compound of formula (I) or (II) wherein R^4 is hydrogen atom and R^3 is hydroxy group can be obtained by subjecting the compound of formula (11) or (12) and the compound of formula (13) to reductive amination reaction in an inert solvent as shown in the scheme below.



As the solvents used in the reaction of the compound of formula (11) or (12) with the compound of formula (13), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran and dioxane; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents and alcohol type solvents may be mentioned.

The compound of formula (I-b) or (II-b) that is the compound of formula (I) or (II) wherein R^4 is hydrogen atom and R^3 is hydroxy group, m is 1, V is CR^7OH can be obtained by reacting the compound of formula (11) or (12) with the compound of formula (14) in an inert solvent as shown in the scheme below.



As the solvents used in the reaction of the compound of formula (11) or (12) with the compound of formula (14), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran and dioxane; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents, nitrile type solvents and alcohol type solvents may be mentioned.

The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 100°C.

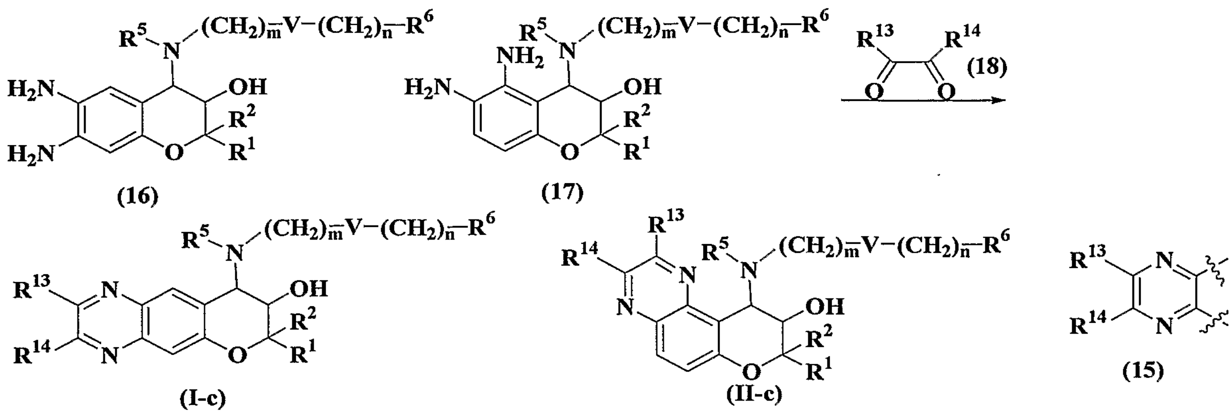
The molar ratio of the reaction materials is within the range of 0.5-4.0, preferably 1.0-2.0, for compound (14)/compound (11) or (12).

The acid catalysts used include inorganic acids exemplified by hydrochloric acid and sulfuric acid, Lewis acids exemplified by aluminum chloride, titanium tetrachloride, boron trifluoride diethylether complex, perchloric acid, lithium perchlorate, lithium bromide and ytterbium trifluoromethanesulfonate.

Preferable acid catalysts are lithium bromide and lithium perchlorate.

The compound of formula (I-c) or (II-c) that is the compound of formula (I) or (II) wherein R^4 is hydrogen atom, R^3 is hydroxy group and A is the group of formula (15) can be also obtained by reacting the compound of formula (16) or (17) with the

compound of formula (18) in an inert solvent as shown in the scheme below.



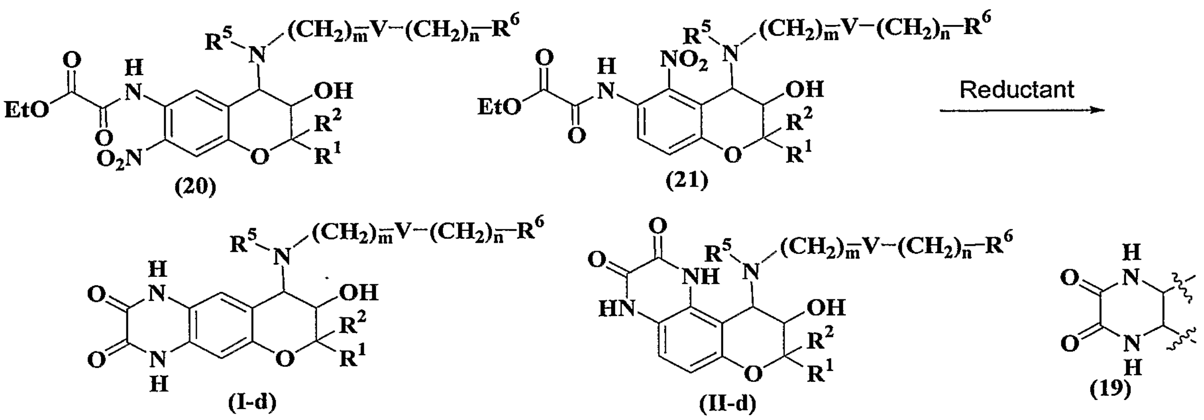
As the solvents used in the reaction of the compound of formula (16) or (17) with the compound of formula (18), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran and dioxane; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, alcohol type solvents may be mentioned.

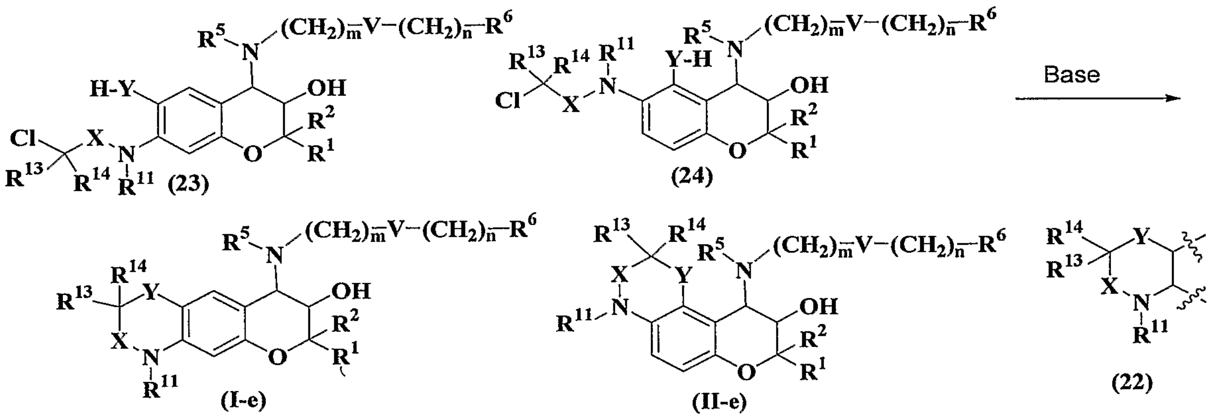
The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 50°C.

The molar ratio of the reaction materials is within the range of 0.5-4.0, preferably 0.8-2.0, for compound (18)/compound (16) or (17).

The compound of formula (I-d) or (II-d) that is the compound of formula (I) or (II) wherein R^4 is hydrogen atom, R^3 is hydroxy group and A is the group of formula (19) can be also obtained by subjecting the compound of formula (20) or (21) to reduction reaction in an inert solvent as shown in the scheme below.



The compound of formula (I-e) or (II-e) that is the compound of formula (I) or (II) wherein R^4 is hydrogen atom, R^3 is hydroxy group and A is the group of formula (22) (X is SO_2 or CO, and Y is S or O) can be also obtained by subjecting the compound of formula (23) or (24) to ring-closure reaction in an inert solvent under basic conditions as shown in the scheme below.



The compounds of formula (I) or (II) that are not included in the compounds of formula (I-a to I-e) and (II-a to II-e), that is, the compounds of formula (I) or (II) wherein R^3 and R^4 are together a bond, or R^4 is hydrogen atom and R^3 is C_{1-6} alkylcarbonyloxy group, can be produced by a preparation process similarly to that described in Japanese Patent Laid-open Nos. Sho 52-91866 and Hei 10-87650.

As described above, the inventors of the present invention found that the compound of formula (I) or (II) has a strong prolongation effect on the refractory period. The prolongation effect on the refractory period is one of mechanisms of anti-arrhythmic action and is an important indicator that can be taken in judging the effectiveness in clinical arrhythmia. Conventional anti-arrhythmic agents having the prolongation effect on the refractory period as the main mechanism (such as d-sotalol belonging to Class III of the antiarrhythmic agent classification according to Vaughan

Williams) have been the therapeutic problems in inducing highly dangerous arrhythmia leading to the sudden death from such as *torsades de pointes* among others due to prolongation of action potential in ventricular muscle correlated to the prolongation effect on the refractory period, and thus becoming the therapeutic problem in arrhythmia mainly of atrial muscle (such as supraventricular tachycardia, atrial flutter, atrial fibrillation and the like).

In order to solve the problems, the inventors of the present invention carried out the investigation of compounds having the prolongation effect on the refractory period selective for atrium muscle than for ventricular muscle, and found that the compound of formula (I) or (II) has a prolongation effect on the refractory period selective for atrium muscle without any influence on the refractory period and action potential in ventricular muscle. The difference between the findings by the inventors and the prior art is in providing the prolongation effect on the refractory period selective for atrium muscle to these compound group, which may be shown by the facts that there is no influence on the action potential duration period of isolated ventricular muscle and there is no influence on QT in the electrocardiogram of anesthetized animal. From above, the compounds of the present invention show no inducing action of arrhythmia in ventricular muscle, thus they can contribute to much safer use in arrhythmia mainly of atrial muscle in comparison with the prior art. The present technical knowledge is beneficial for therapeutic or preventive uses as anti-atrial fibrillation agents, anti-atrial flutter agents and anti-atrial tachycardia agents relating to paroxysmal, chronic, preoperative, intraoperative or postoperative atrial arrhythmia, prevention in the progression leading to embolus due to arrhythmia of artial nature, prevention in the progression leading to ventricular arrhythmia or tachycardia from atrial arrhythmia or tachycardia, and averting the life threatening prognosis due to preventive action on atrial arrhythmia or tachycardia leading to ventricular arrhythmia or tachycardia.

The present invention provides a pharmaceutical composition or a veterinary pharmaceutical composition containing a compound of formula (I) or (II) in an effective amount for these treatments.

As forms of administration for the compound according to the present invention, parenteral administration forms such as injections (subcutaneous, intravenous, intramuscular and intraperitoneal injections), ointments, suppositories, aerosols and the like, and oral administration forms such as tablets, capsules, granules, pills, syrups, solutions, emulsions, suspensions and the like can be

mentioned.

The pharmaceutical or veterinary pharmaceutical composition described above contains the compound according to the present invention in an amount of about 0.01-99.5%, preferably about 0.1-30%, based on the total weight of the composition.

In addition to the compound according to the present invention or the composition containing the compound, other pharmaceutically or veterinary pharmaceutically active compounds may be contained.

Further, these compositions may contain the plurality of compounds according to the present invention.

An amount of the compound according to the present invention to be used in clinical administration may vary depending on age, weight and sensitivity of the patient, symptomatic condition and the like, but an effective amount in clinical administration is generally about 0.003-1.5 g, preferably 0.01-0.6 g, per day for adult. If necessary, however, the amount outside of the aforementioned range may be used.

The compound according to the present invention is formulated for administration by conventional pharmaceutical means.

That is, tablets, capsules, granules and pills for oral administration are prepared by using excipients such as sucrose, lactose, glucose, starch and mannitol; binders such as hydroxypropyl cellulose, syrup, gum arabic, gelatin, sorbitol, tragacanth, methyl cellulose and polyvinyl pyrrolidone; disintegrators such as starch, carboxymethyl cellulose or its calcium salt, microcrystalline cellulose and polyethylene glycol; lubricants such as talc, magnesium or calcium stearate, and silica; lubricaing agents such as sodium laurate and glycerol and the like.

Injections, solutions, emulsions, suspensions, syrups and aerosols are prepared by using solvents for the active components such as water, ethyl alcohol, isopropyl alcohol, propylene glycol, 1,3-butylene glycol and polyethylene glycol; surfactants such as sorbitan fatty acid ester, polyoxyethylene sorbitan fatty acid ester, polyoxyethylene fatty acid ester, polyoxyethylene ether of hydrogenated castor oil and lecithin; suspending agents such as carboxymethyl sodium salt, cellulose derivatives such as methyl cellulose or the like, and natural rubbers such as gum arabic, tragacanth or the like; and preserves such as p-hydroxybenzoic acid esters, benzalkonium chloride, sorbic acid salts and the like.

For ointments that are transdermally adsorptive pharmaceutics, for example, white vaseline, liquid paraffin, higher alcohols, Macrogol ointments, hydrophilic

ointments, aqueous gel-type bases and the like are used.

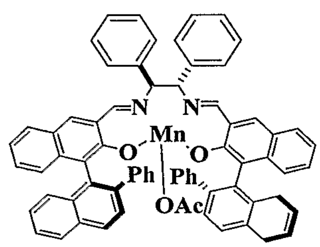
Suppositories are prepared by using, for example, cocoa fats, polyethylene glycol, lanolin, fatty acid triglyceride, coconut oil, polysorbate and the like.

Examples

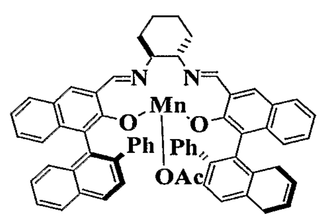
The present invention is illustrated in detail by the Examples as follows, but the present invention is not limited to these Examples.

[Synthesis Examples]

Furthermore, Ph,Ph salen manganese complex (XX) and Cyc,Ph salen manganese complex (XY) mean optically active compounds of formula below which were synthesized according to the method similar to one described in Japanese Patent Laid-open No. Hei 7-285983.



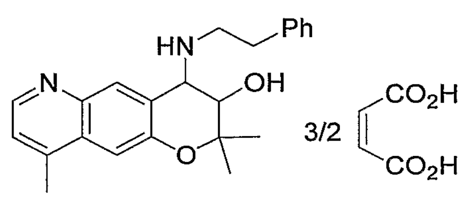
(XX)



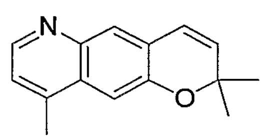
(XY)

Synthesis Example 1

(±)-*trans*-2,2,9-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 3/2 maleate



2,2,9-Trimethyl-2*H*-pyrano[2,3-g]quinoline



To a solution of 6-amino-2,2-dimethylchromene (10.1 g, 57.7 mmol) in ethanol (500 mL), methylvinylketone (33.0 mL, 404 mmol), *m*-nitrobenzenesulfonic acid (21.1 g, 104 mmol), zinc chloride (1.97 g, 14.4 mol) and 35% hydrochloric acid (24 mL, 289

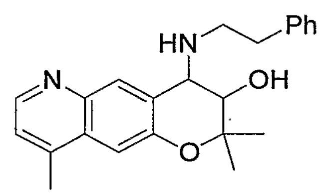
mmol) were added at room temperature and the resulting mixture was stirred at 110°C for 5 hours. Upon the completion of the reaction, ethanol was distilled off, water was added, and the resulting solution was neutralized with sodium hydrogencarbonate and extracted with ethyl acetate. The resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 3/1) and the aimed product was obtained (yield: 38%).

Brown amorphous product

^{1}H-NMR($CDCl_3$) δ; 1.51(s, 6H), 2.59(d, J = 0.6 Hz, 3H), 5.90(d, J = 9.9 Hz, 1H), 6,59(d, J = 9.9 Hz, 1H), 7.11(d, J = 3.6 Hz, 1H), 7.25(s, 1H), 7.68(s, 1H), 8.57(d, J = 4.4 Hz, 1H)

MS(ESI$^+$)m/z; 226 $[M+1]^+$

(±)-*trans*-2,2,9-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



To a solution of 2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline (530 mg, 2.35 mmol) in dimethylsulfoxide (8 mL), *N*-bromosuccinimide (920 mg, 5.17 mmol) and water (1.6 mL) were added at room temperature and the resulting mixture was stirred at room temperature for 3 hours. Upon the completion of the reaction, water was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. Aqueous sodium hydrogencarbonate solution was added to the aqueous phase and the resulting solution was further extracted with ethyl acetate. The combined organic phases were was dried over anhydrous magnesium sulfate and the solvent was distilled off to obtain a crude product of (±)-*trans*-3-bromo-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-ol. At room temperature, 1,4-dioxane (30 mL) and 1 mol/L aqueous sodium hydroxide solution (5.64 mL) were added thereto, and the resulting solution was stirred at room temperature for 2.5 hours. Upon the completion of the reaction, water was added to the reaction solution, and the resulting solution was extracted with ethyl acetate, dried over anhydrous magnesium sulfate and the solvent was distilled off to obtain a crude

product of 3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline. To the residue, 1,4-dioxane (3.2 mL), lithium perchlorate (250 mg, 2.35 mmol) and 2-phenylethylamine (0.35 mL, 2.82 mmol) were added at room temperature, and the resulting mixture was stirred at 75°C for 5 hours. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the resulting solution was extracted with ethyl acetate, the organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 1/1) and the aimed product was obtained (3-steps, yield: 26%).

^{1}H-NMR($CDCl_3$) δ; 1.26(s, 3H), 1.55(s, 3H), 2.59(s, 3H), 2.83(t, J = 6.8 Hz, 2H), 2.96-3.12(m, 3H), 3.60(d, J = 10.5 Hz, 1H), 3.88(dd, J = 1.1 Hz, 10.5 Hz, 1H), 7.13(d, J = 4.2 Hz, 1H), 7.18-7.32(m, 6H), 7.98(d, J = 1.1 Hz, 1H), 8.60(d, J = 4.4 Hz, 1H)

MS(ESI$^+$)m/z; 363 $[M+1]^+$

To a solution of (±)-*trans*-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol (219 mg, 0.60 mmol) in ethyl acetate (3 mL), a solution of maleic acid (77 mg, 0.66 mmol) in ethyl acetate (1 mL) was added dropwise, the resulting reaction solution was cooled to 0°C, hexane (10 mL) was added thereto, and precipitated solid was filtered off to obtain (±)-*trans*-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 3/2 maleate (yield: 72%).

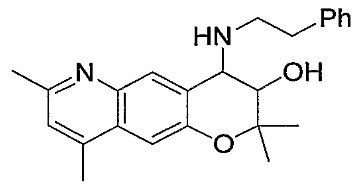
Yellow crystals

mp;172-174°C (decomposition)

^{1}H-NMR(DMSO-d_6) δ; 1.17(s, 3H), 1.50(s, 3H), 2.59(s, 3H), 2.94-3.37(m, 4H), 4.10(dd, J = 6.1 Hz, 9.4 Hz, 1H), 4.72(d, J = 9.4 Hz, 1H), 6.09(s, 3H), 6.33(d, J = 6.1 Hz, 1H), 7.23-7.35(m, 6H), 7.42(s, 1H), 8.43(s, 1H), 8.66(d, J = 4.1 Hz, 1H)

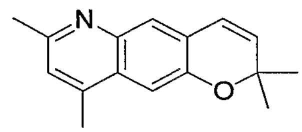
Synthesis Example 2

(±)-*trans*-2,2,7,9-Tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



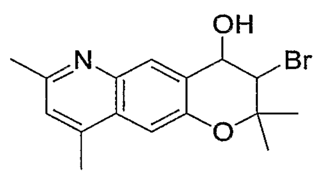
This compound was synthesized according to the process of Synthesis Example 1.

2,2,7,9-Tetramethyl-2*H*-pyrano[2,3-g]quinoline



(Yield: 59%)
Black brown oily product
^{1}H-NMR($CDCl_3$) δ: 1.49(s, 6H), 2.54(s, 3H), 2.62(s, 3H), 5.86(d, *J* = 9.9 Hz, 1H), 6,55(d, *J* = 9.9 Hz, 1H), 7.00(s, 1H), 7.20(s, 1H), 7.60(s, 1H)
MS(ESI$^+$)m/z; 240[M+1]$^+$

(±)-*trans*-3-Bromo-2,2,7,9-tetramethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-ol



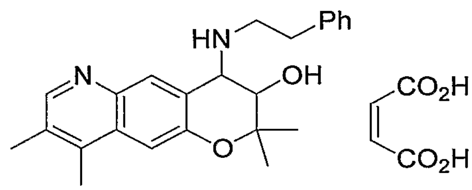
(Yield: 82%)
^{1}H-NMR($CDCl_3$) δ; 1.47(s, 3H), 1.68(s, 3H), 2.58(s, 3H), 2.70(s, 3H), 4.28(d, *J* = 9.6 Hz, 1H), 5.14(d, *J* = 9.6 Hz, 1H), 7.08(s, 1H), 7.28(s, 1H), 8.37(s, 1H)
MS(ESI$^+$)m/z; 336, 338 [M+1]$^+$

(±)-*trans*-2,2,7,9-Tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol (yield: 17%)
White crystals
mp;144-147°C
^{1}H-NMR($CDCl_3$) δ; 1.25(s, 3H), 1.54(s, 3H), 1.90(br s, 1H), 2.55(s, 3H), 2.65(s, 3H), 2.81(t, *J* = 6.8 Hz, 2H), 2.97-3.10(m, 2H), 3.19(br s, 1H), 3.58(d, *J* = 10.5 Hz, 1H), 3.85(d, *J* = 10.5 Hz, 1H), 7.04(s, 1H), 7.17-7.31(m, 6H), 7.91(s, 1H)
MS(ESI$^+$)m/z; 377 [M+1]$^+$

MS(ESI$^-$)m/z; 421 [M+45]$^+$ (HCOOH adduct)

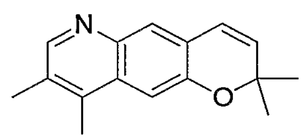
Synthesis Example 3

(±)-*trans*-2,2,8,9-Tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



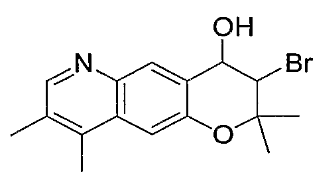
This compound was synthesized according to the process of Synthesis Example 1.

2,2,8,9-Tetramethyl-2*H*-pyrano[2,3-g]quinoline



(Yield: 50%)
^{1}H-NMR($CDCl_3$) δ; 1.50(s, 6H), 2.50(s, 3H), 2.66(s, 3H), 5.87(d, *J* = 9.9 Hz, 1H), 6,57(d, *J* = 9.9 Hz, 1H), 7.26(s, 1H), 7.63(s, 1H), 8.48(s, 1H)
MS(ESI$^+$)m/z; 240 [M+1]$^+$

(±)-*trans*-3-Bromo-2,2,7,9-tetramethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-ol

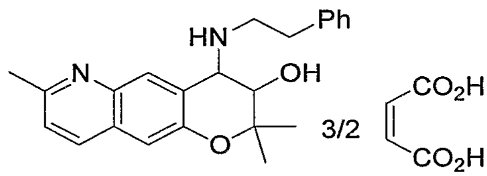


(Yield: 65%)
^{1}H-NMR($CDCl_3$) δ; 1.48(s, 3H), 1.69(s, 3H), 1.80(br s, 1H), 2.46(s, 3H), 2.56(s, 3H), 4.28(d, *J* = 9.6 Hz, 1H), 5.15(d, *J* = 9.6 Hz, 1H), 7.25(s, 1H), 8.42(s, 1H), 8.57(s, 1H)
MS(ESI$^+$)m/z; 336, 338 [M+1]$^+$

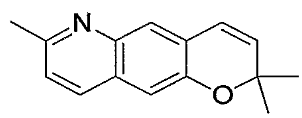
(±)-*trans*-2,2,8,9-Tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol·1 maleate
(Yield: 4%)
White crystals

mp;199-203°C
^{1}H-NMR(DMSO-d_6) δ; 1.17(s, 3H), 1.50(s, 3H), 2.41(s, 3H), 2.49(s, 3H), 2.89-3.40(m, 4H), 4.07(dd, J = 5.5 Hz, 9.4 Hz, 1H), 4.66(d, J = 9.4 Hz, 1H), 6.05(s, 2H), 6.28(d, J = 5.5 Hz, 1H), 7.22-7.35(m, 5H), 7.43(s, 1H), 8.36(s, 1H), 8.59(s, 1H)
MS(ESI$^+$)m/z; 377 [M+1]$^+$
MS(ESI$^-$)m/z; 421 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 4
(±)-*trans*-2,2,7-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 3/2 maleate

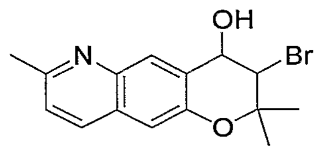


2,2,7-Trimethyl-2*H*-pyrano[2,3-g]quinoline



To 6-amino-2,2-dimethylchromene (1.00 g, 5.71 mmol), 35% hydrochloric acid (1.43 mL, 17.1 mmol), *p*-chloranil (1.40 g, 5.71 mmol) and *n*-butanol (1.3 mL) were added at room temperature and the temperature was increased to 120°C. A solution of crotyl aldehyde (0.567 mL, 6.84 mmol) in *n*-butanol (0.52 mL) was added and the resulting mixture was stirred at 120°C for 20 minutes. A solution of zinc chloride (0.777 g, 5.71 mmol) in tetrahydrofuran (10 mL) was added, and the resulting mixture was stirred at 120°C for 20 minutes. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added, and the resulting solution was extracted with ethyl acetate and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 2/1), and recrystallized from ethyl acetate to obtain the aimed product (yield: 22%).
Gray solid
^{1}H-NMR($CDCl_3$) δ; 1.48(s, 6H), 2.67(s, 3H), 5.87(d, J = 9.9 Hz, 1H), 6,55(d, J = 9.9 Hz, 1H), 7.05(s, 1H), 7.16(d, J = 8.5 Hz, 1H), 7.64(s, 1H), 7.86(d, J = 8.5 Hz, 1H)
MS(ESI$^+$)m/z; 226 [M+1]$^+$
MS(ESI$^-$)m/z; 225 [M]$^+$

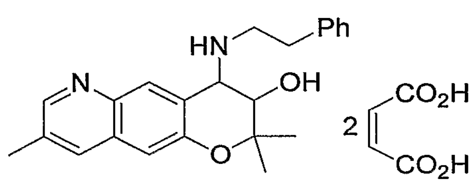
(±)-*trans*-3-Bromo-2,2,7-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-ol



This compound was synthesized according to the process of Synthesis Example 1.
(Yield: 24%)

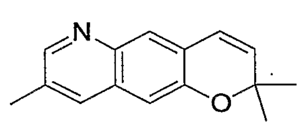
(±)-*trans*-2,2,7-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 3/2 maleate
(Yield: 12%)
White crystals
^{1}H-NMR(DMSO-d_6) δ; 1.15(s, 3H), 1.48(s, 3H), 2.63(s, 3H), 2.70-3.38(m, 4H), 4.09(dd, J = 5.8 Hz, 9.4 Hz, 1H), 4.68(d, J = 9.4 Hz, 1H), 6.08(s, 3H), 6.29(d, J = 5.8 Hz, 1H), 7.22-7.35(m, 6H), 7.40(s, 1H), 8.10(d, J = 8.5 Hz, 1H), 8.33(s, 1H)
MS(ESI$^+$)m/z; 363 [M+1]$^+$
MS(ESI$^-$)m/z; 407 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 5
(±)-*trans*-2,2,8-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 2 maleate



This compound was synthesized according to the process of Synthesis Example 4.

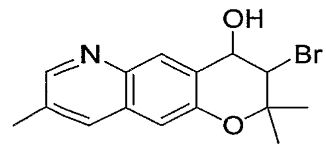
2,2,8-Trimethyl-2*H*-pyrano[2,3-g]quinoline



(Yield: 17%)

^{1}H-NMR($CDCl_3$) δ; 1.48(s, 6H), 2.45(s, 3H), 5.87(d, J = 9.9 Hz, 1H), 6.56(d, J = 9.9 Hz, 1H), 7.00(s, 1H), 7.64(s, 1H), 7.70(s, 1H), 8.54(d, J = 8.5 Hz, 1H)
MS(ESI$^+$)m/z; 226 [M+1]$^+$

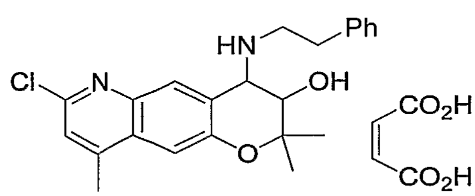
(±)-*trans*-3-Bromo-2,2,8-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-ol



(Yield: 54%)
MS(ESI$^+$)m/z; 322, 324 [M+1]$^+$

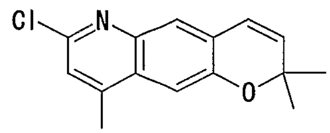
(±)-*trans*-2,2,8-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 2 maleate
(Yield: 20%)
White crystals
^{1}H-NMR(DMSO-d_6) δ; 1.15(s, 3H), 1.49(s, 3H), 2.45(s, 3H), 2.97-3.39(m, 4H), 4.09(dd, J = 6.1 Hz, 9.4 Hz, 1H), 4.71(d, J = 9.1 Hz, 1H), 6.15(s, 4H), 6.32(d, J = 6.3 Hz, 1H), 7.19-7.36(m, 5H), 7.97(s, 1H), 8.39(s, 1H), 8.67(s, 1H)

Synthesis Example 6
(±)-*trans*-7-Chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



To a solution of 2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline (1.56 g, 6.92 mmol) in chloroform (15.6 mL), a solution of *m*-chloroperbenzoic acid (2.61 g, 15.2 mmol) in chloroform (6.4 mL)-methanol (1.6 mL) was added dropwise at room temperature and the resulting mixture was stirred at room temperature for 1.5 hour. Upon the completion of the reaction, the reaction solution was extracted with aqueous sodium thiosulfate solution and the resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, chloroform

(33 mL), *p*-toluenesulfonyl chloride (1.32 g, 6.92 mmol) and potassium carbonate (0.954 g, 6.92 mmol) were added to the residue at room temperature, and the resulting mixture was stirred at 70°C for 3 hours. Upon the completion of the reaction, water was added to the reaction solution, and it was extracted with chloroform. The resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 2/1) and the aimed product was obtained (yield: 67%).

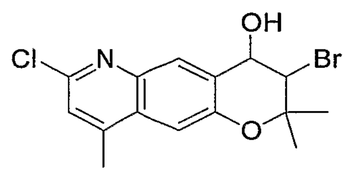


Pale yellow solid

^{1}H-NMR($CDCl_3$) δ; 1.42(s, 6H), 2.48(d, *J* = 0.8 Hz, 3H), 5.83(d, *J* = 9.9 Hz, 1H), 6.47(d, *J* = 9.9 Hz, 1H), 7.03(d, *J* = 3.6 Hz, 1H), 7.11(s, 1H), 7.50(s, 1H)

MS(ESI$^+$)m/z; 260 [M+1]$^+$

(±)-*trans*-3-Bromo-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-ol



Hereinafter, the aimed compound was synthesized according to the process of Synthesis Example 1.

(Yield: 44%)

MS(ESI$^+$)m/z; 356, 358 [M+1]$^+$

(±)-*trans*-7-Chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate

(Yield: 58%)

White crystals

mp: 221-226°C (decomposition)

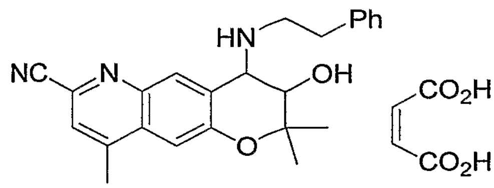
^{1}H-NMR(DMSO-d_6) δ; 1.17(s, 3H), 1.49(s, 3H), 2.60(s, 3H), 2.93-3.32(m, 4H), 4.05(m, 1H), 4.65(d, *J* = 9.4 Hz, 1H), 6.05(s, 2H), 6.28(br s, 1H), 7.22-7.34(m, 5H), 7.43(s, 2H), 8.32(s, 1H)

MS(ESI$^+$)m/z; 397 [M+1]$^+$

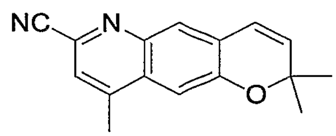
MS(ESI$^-$)m/z; 441 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 7

(±)-*trans*-3-Hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile 1 maleate



2,2,9-Trimethyl-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile



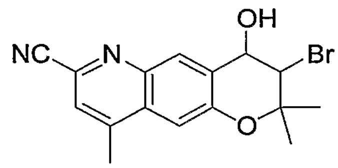
To a solution of 2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline (4.36 g, 19.3 mmol) in chloroform (43.6 mL), a solution of *m*-chloroperbenzoic acid (7.35 g, 42.6 mmol) in chloroform (17.4 mL)-methanol (4.36 mL) was added dropwise at room temperature and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, the reaction solution was extracted with aqueous sodium thiosulfate solution and the resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, acetonitrile (19.3 mL), trimethylsilylcyanide (7.27 mL, 57.9 mmol) and triethylamine (5.38 mL, 38.6 mmol) were added to the residue at room temperature, and the resulting solution was stirred at 70°C for 3.5 hours. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and it was extracted with chloroform and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 2/1) and the aimed product was obtained (yield: 55%).

Pale yellow solid

^{1}H-NMR(CDCl$_3$) δ; 1.52(s, 6H), 2.62(d, *J* = 0.6 Hz, 3H), 5.97(d, *J* = 9.9 Hz, 1H), 6.58(d, *J* = 9.9 Hz, 1H), 7.23(s, 1H), 7.40(s, 1H), 7.71(s, 1H)

MS(ESI$^+$)m/z; 251 [M+1]$^+$

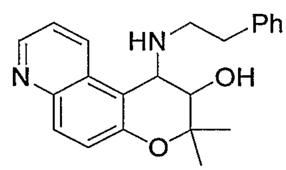
(±)-*trans*-3-Bromo-4-hydroxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile



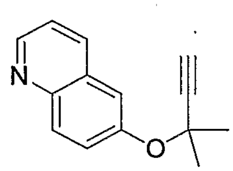
Hereinafter, the aimed compound was synthesized according to the process of Synthesis Example 1.
(Yield: 36%)
MS(ESI$^+$)m/z; 349 [M+1]$^+$

(±)-*trans*-3-Hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile 1 maleate
White crystals
mp: 218-220°C (decomposition)
^{1}H-NMR(DMSO-d$_6$) δ; 1.20(s, 3H), 1.51(s, 3H), 2.65(s, 3H), 2.96-3.33(m, 4H), 4.04-4.06(m, 1H), 4.64(br s, 1H), 6.05(s, 2H), 6.29 (br s, 1H), 7.25-7.31(m, 5H), 7.50(s, 1H), 7.85(s, 1H), 8.49(s, 1H)
MS(ESI$^+$)m/z; 388 [M+1]$^+$
MS(ESI$^-$)m/z; 432 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 8
(±)-*trans*-3,3-Dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinolin-2-ol



6-[(1,1-dimethyl-2-propynyl)oxy]quinoline



A solution of 2-methyl-3-butyn-2-ol (2.45 mL, 25.1 mmol) and 1,8-diazabicyclo-[5.4.0]-7-undecene (4.25 mL, 28.4 mmol) in acetonitrile (15.5 mL) was stirred 0°C for 30 minutes, and trifluoroacetic anhydride (3.55 mL, 25.1 mmol) was added dropwise. The resulting mixture was added dropwise to a mixed solution

of 6-hydroxyquinoline (2.43 g, 16.7 mmol), copper (I) chloride (8.3 mg, 0.0835 mmol), acetonitrile (15.5 mL) and 1,8-diazabicyclo-[5.4.0]-7-undecene (4.25 mL, 28.4 mmol) at 0°C, and stirred at 0°C for 3 hours. The resulting solution was acidified with 1 mol/L HCl and extracted with ethyl acetate, and the resulting aqueous phase was neutralized with aqueous sodium hydrogencarbonate solution, extracted with ethyl acetate, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 1/1 to 1/3) and the aimed product was obtained.

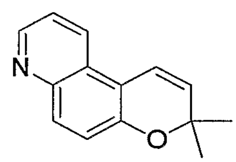
Pale yellow solid

mp: 65-67°C

^{1}H-NMR($CDCl_3$) δ; 1.86(s, 6H), 2.70(s, 1H), 7.69-7.71(2H), 7.80(s, 1H), 8.33(d, *J* = 8.3 Hz, 1H), 8.45(d, *J* = 8.3 Hz 1H), 9.01(br s, 1H)

MS(GC)m/z; 211 $[M]^+$

3,3-Dimethyl-3*H*-pyrano[3,2-f]quinoline



A solution of 6-[(1,1-dimethyl-2-propynyl)oxy]quinoline (16.7 mmol) in 1,2-dichlorobenzene (10 mL) was stirred at 180°C for 1 hour. Upon the completion of the reaction, the solvent was distilled off, and the residue was recrystallized from hexane-ethyl acetate to obtain the aimed compound (2-steps, quant.).

Green crystals

mp: 104-107°C

^{1}H-NMR($CDCl_3$) δ; 1.54(s, 6H), 5.89(d, *J* = 10.2 Hz, 1H), 6.93(d, *J* = 10.2 Hz, 1H), 7.50(d, *J* = 9.1 Hz, 1H), 7.73(br s, 1H), 8.31(d, *J* = 9.1 Hz, 1H), 8.74(d, *J* = 8.5 Hz, 1H), 9.03(br s, 1H)

MS(GC)m/z; 211$[M]^+$

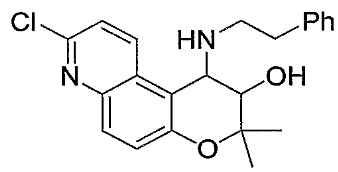
(±)-*trans*-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinolin-2-ol

Hereinafter, the aimed compound was synthesized according to the process of Synthesis Example 1.

mp: 180-182°C

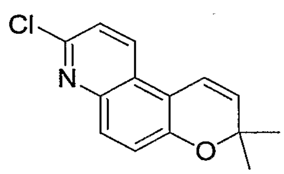
^{1}H-NMR($CDCl_3$) δ; 1.32(s, 3H), 1.44(s, 3H), 1.63(br s, 1H), 2.43(br s, 1H), 2.69-2.84(m, 3H), 2.92-2.97(m, 1H), 3.83(d, J = 5.0 Hz, 1H), 4.09(d, J = 5.5 Hz, 1 H), 7.10-7.29(m, 6H), 7.86(d, J = 9.1 Hz, 1H), 8.13(d, J = 7.7 Hz, 1H), 8.71(dd, J = 1.7 Hz, 4.1 Hz, 1H)
MS(ESI$^+$)m/z; 349 [M+1]$^+$
MS(ESI$^-$)m/z; 393 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 9
(±)-*trans*-8-Chloro-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f] quinolin-2-ol



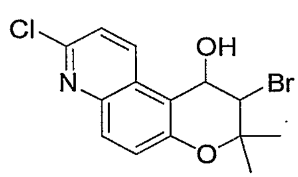
By use of 3,3-dimethyl-3*H*-pyrano[3,2-f]quinoline, the aimed compound was synthesized similarly to the process of Synthesis Example 6.

8-Chloro-3,3-dimethyl-3*H*-pyrano[3,2-f]quinoline



(Yield: 82%)
Red-brown oily product
^{1}H-NMR($CDCl_3$) δ; 1.49(s, 6H), 5.77(d, J = 9.9 Hz, 1H), 6.87(d, J = 9.9 Hz, 1H), 7.27(d, J = 9.1 Hz, 1H), 7.34(d, J = 8.8 Hz, 1H), 7.80(d, J = 9.1 Hz, 1H), 8.19(d, J = 8.8 Hz, 1H)
MS(ESI$^+$)m/z; 246 [M+1]$^+$

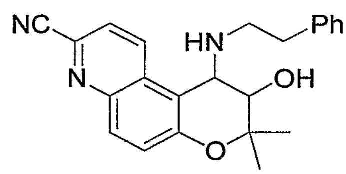
(±)-*trans*-2-Bromo-8-chloro-3,3-dimethyl-2,3-dihydro-1*H*-pyrano[3,2-f]quinolin-1-ol



(Yield: 45%)

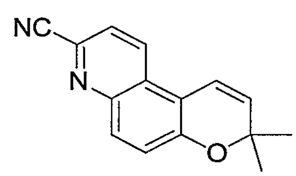
(±)-*trans*-8-Chloro-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinolin-2-ol
(Yield: 60%)
White crystals
mp: 141-143°C
^{1}H-NMR($CDCl_3$) δ; 1.28(s, 3H), 1.44(s, 3H), 1.64(br s, 2H), 2.65-2.78(m, 3H), 2.86-2.96(m, 1H), 3.84(d, J = 6.1 Hz, 1H), 4.06(d, J = 5.8 Hz, 1H), 7.08-7.30(m, 7H), 7.98(d, J = 9.1 Hz, 1H), 8.22(d, J = 8.8 Hz, 1H)
MS(ESI$^+$)m/z; 383 [M+1]$^+$
MS(ESI$^-$)m/z; 427 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 10
(±)-*trans*-2-Hydroxy-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinoline-8-carbonitrile



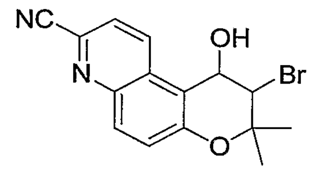
By use of 3,3-dimethyl-3*H*-pyrano[3,2-f]quinoline, the aimed compound was synthesized similarly to the process of Synthesis Example 7.

3,3-Dimethyl-3*H*-pyrano[3,2-f]quinoline-8-carbonitrile



(Yield: quant.)
Yellow solid
^{1}H-NMR($CDCl_3$) δ; 1.52(s, 6H), 5.80(d, J = 9.9 Hz, 1H), 6.89(d, J = 10.2 Hz, 1H), 7.37(d, J = 9.4 Hz, 1H), 7.65(d, J = 8.8 Hz, 1H), 7.95(d, J = 9.4 Hz, 1H), 8.64(d, J = 8.8 Hz, 1H)
MS(ESI$^+$)m/z; 237 [M+1]$^+$
MS(ESI$^-$)m/z; 235 [M-1]$^+$

(±)-*trans*-2-Bromo-1-hydroxy-3,3-dimethyl-2,3-dihydro-1*H*-pyrano[3,2-f]quinoline-8-carbonitrile



(Yield: 49%)

^{1}H-NMR($CDCl_3$) δ; 1.50(s, 3H), 1.69(s, 3H), 2.72(d, *J* = 4.1 Hz, 1H), 4.35(d, *J* = 7.2 Hz, 1H), 5.43(dd, *J* = 3.9 Hz, 7.2 Hz, 1H), 7.36(d, *J* = 9.1 Hz, 1H), 7.70(d, *J* = 8.8 Hz, 1H), 8.03(d, *J* = 9.4 Hz, 1H), 8.72(d, *J* = 8.5 Hz, 1H)

MS(ESI$^+$)m/z; 333, 335 [M+1]$^+$

MS(ESI$^-$)m/z; 379 [M+45]$^+$ (HCOOH adduct)

(±)-*trans*-2-Hydroxy-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinoline-8-carbonitrile

(Yield: 72%)

White crystals

mp: 93-96°C

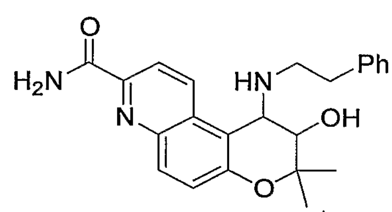
^{1}H-NMR($CDCl_3$) δ; 1.30(s, 3H), 1.46(s, 3H), 1.60(br s, 3H), 2.13(br s, 1H), 2.66-2.79(m, 3H), 2.88-2.98(m, 1H), 3.87(d, *J* = 5.8 Hz, 1H), 4.08(d, *J* = 6.1 Hz, 1H), 7.09(d, *J* = 6.3 Hz, 1H), 7.10(d, *J* = 7.4 Hz, 1H), 7.23-7.27(m, 3H), 7.30(d, *J* = 9.1 Hz, 1H), 7.41(d, *J* = 8.8 Hz, 1H), 7.92(d, *J* = 9.1 Hz, 1H), 8.38(d, *J* = 8.5 Hz, 1H)

MS(ESI$^+$)m/z; 374 [M+1]$^+$

MS(ESI$^-$)m/z; 418 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 11

(±)-*trans*-2-Hydroxy-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinoline-8-carboxamide



To a solution of (±)-*trans*-2-hydroxy-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f

]quinoline-8-carbonitrile (400 mg, 1.07 mmol) in *t*-butanol (40 mL), potassium hydroxide (800 mg, 14.3 mmol) was added at room temperature and the resulting mixture was stirred at 90°C for 2 hour. Upon the completion of the reaction, aqueous sodium chloride solution was added to the reaction solution, and it was extracted with ethyl acetate and the resulting organic phase was dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 1/1) and recrystallized from hexane-ethyl acetate to obtain the aimed product (yield: 54%).

White crystals

mp: 197-199°C

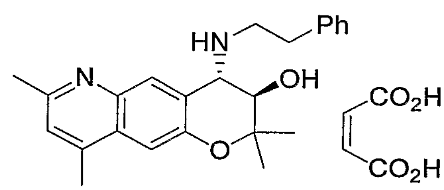
^{1}H-NMR($CDCl_3$) δ; 1.32(s, 3H), 1.47(s, 3H), 1.71(br s, 2H), 2.29(br s, 1H), 2.69-2.76(m, 3H), 2.89-2.97(m, 1H), 3.86(br s, 1H), 4.13(d, *J* = 5.8 Hz, 1H), 5.62(br s, 1H), 7.10(d, *J* = 6.9 Hz, 1H), 7.10(d, *J* = 7.4 Hz, 1H), 7.20-7.28(m, 4H), 7.89(d, *J* = 9.4 Hz, 1H), 7.98(br s, 1H), 8.07(d, *J* = 8.8 Hz, 1H), 8.31(d, *J* = 8.8 Hz, 1H)

MS(ESI$^+$)m/z; 392 [M+1]$^+$

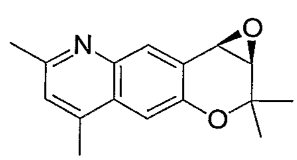
MS(ESI$^-$)m/z; 436 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 12

(*3R*,4S**)-2,2,7,9-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



(*3R*,4R**)-3,4-epoxy-2,2,7,9-tetramethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline



To a solution of 2,2,7,9-tetramethyl-2*H*-pyrano[2,3-g]quinoline (4.64 g, 19.4 mmol) in ethyl acetate (70 mL), *N*-methyl imidazole (0.303 mL, 3.88 mmol) and Ph,Ph salen manganese complex (XX) (201 mg, 0.194 mmol) were added at room temperature and aqueous sodium hypochlorite solution (25.6 g, 1.513 mol/kg, 38.8 mmol) was added dropwise, and the resulting mixture was stirred for 1 hour. Further, in water bath, aqueous sodium hypochlorite solution (25.6 g, 1.513 mol/kg, 38.8

mmol) was added, and the resulting mixture was stirred in water bath for 1 hour. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added to the reaction solution, the resulting mixture was filtered through celite and extracted. The organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 1/3) and the aimed product was obtained (yield: 68%).

> 99.9% ee; CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 5.7 min.

^{1}H-NMR($CDCl_3$) δ; 1.30(s, 3H), 1.64(s, 3H), 2.56(s, 3H), 2.66(s, 3H), 3.59(d, *J* = 4.4 Hz, 1H), 4.14(d, *J* = 4.4 Hz, 1H), 7.08(s, 1H), 7.29(s, 1H), 8.04(s, 1H)

MS(ESI$^+$)m/z; 256 [M+1]$^+$

(*3R*,4S**)-2,2,7,9-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate

To a solution of (*3R*,4R**)-3,4-epoxy-2,2,7,9-tetramethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline (0.80 g, 3.14 mmol) in 1,4-dioxane (1.6 mL), lithium perchlorate (334 mg, 3.14 mmol) and 2-phenylethylamine (0.473 mL, 3.77 mmol) were added at room temperature. and the resulting mixture was stirred at 70°C for 1 hour. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and it was extracted with ethyl acetate and the resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (ethyl acetate). Further, after distilling off the solvent, ethyl acetate (2 mL) was added and a solution of maleic acid (376 mg, 3.23 mmol) in ethyl acetate (8mL) was added dropwise. The resulting precipitated solid was filtered to obtain the aimed product (yield: 86%).

White crystals

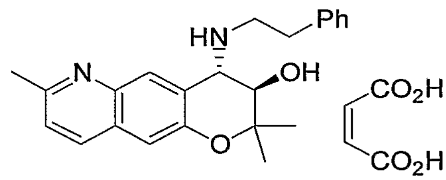
mp: 215-219°C (decomposition)

^{1}H-NMR(DMSO-d_6) δ; 1.16(s, 3H), 1.49(s, 3H), 2.55(s, 3H), 2.58(s, 3H), 2.93-3.39 (m, 4H), 4.07(dd, *J* = 6.4 Hz, 9.4 Hz, 1H), 4.64(d, *J* = 9.4 Hz, 1H), 6.05(s, 2H), 6.27(d, *J* = 5.8 Hz, 1H), 7.24-7.26(m, 4H), 7.30(s, 1H), 7.33(s, 1H), 7.36(s, 1H), 8.31(s, 1H)

MS(ESI$^+$)m/z; 377 [M+1]$^+$

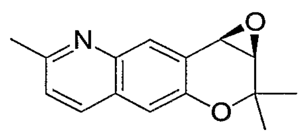
MS(ESI$^-$)m/z; 421 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 13
(*3R*,4S**)-2,2,7-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



This compound was synthesized according to the process of Synthesis Example 12.

(*3R*,4R**)-3,4-epoxy-2,2,7-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline

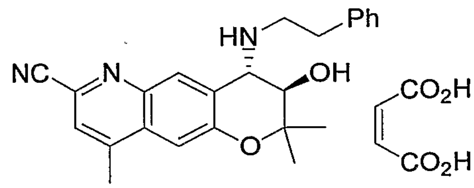


99.3% ee; CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 6.2 min.
^{1}H-NMR($CDCl_3$) δ; 1.28(s, 3H), 1.64(s, 3H), 2.71(s, 3H), 3.59(d, *J* = 4.4 Hz, 1H), 4.15(d, *J* = 4.4 Hz, 1H), 7.13(s, 1H), 7.23(d, *J* = 8.5 Hz, 1H), 7.91(d, *J* = 8.5 Hz, 1H), 8.05(s, 1H)
MS(ESI$^+$)m/z; 242 [M+1]$^+$

(*3R*,4S**)-2,2,7-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate
White crystals
mp: 214-217°C (decomposition)
^{1}H-NMR(DMSO-d_6) δ; 1.15(s, 3H), 1.48(s, 3H), 2.62(s, 3H), 2.93-3.14 (m, 4H), 4.03-4.07(m, 1H), 4.61(br s, 1H), 6.04(s, 2H), 6.23(br s, 1H), 7.23-7.39(m, 7H), 8.09(d, *J* = 8.5 Hz, 1H), 8.31(s, 1H)
MS(ESI$^+$)m/z; 363 [M+1]$^+$
MS(ESI$^-$)m/z; 407 [M+45]$^+$ (HCOOH adduct)

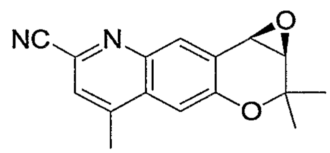
Synthesis Example 14
(*3R*,4S**)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2

,3-g]quinoline-7-carbonitrile 1 maleate



This compound was synthesized according to the process of Synthesis Example 12.

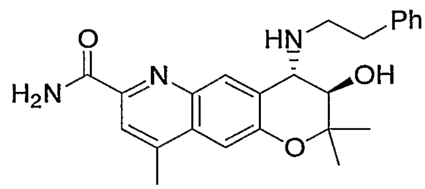
(*3R*,4R**)-3,4-epoxy-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile



(Yield: 33%)
99.1% ee; CHIRALCEL OJ-R acetonitrile/methanol/0.01 M aqueous sodium chloride solution = 1/3/3, Retention time: 18.6 min.
^{1}H-NMR($CDCl_3$) δ; 1.33(s, 3H), 1.66(s, 3H), 2.65(s, 3H), 3.64(d, *J* = 4.1 Hz, 1H), 4.17(d, *J* = 4.4 Hz, 1H), 7.33(s, 1H), 7.47(s, 1H), 8.18(s, 1H)
MS(ESI$^+$)m/z; 267 [M+1]$^+$
MS(ESI$^-$)m/z; 265 [M-1]$^+$

(*3R*,4S**)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile 1 maleate
(Yield: 23%)
Pale brown crystals
^{1}H-NMR(DMSO-d_6) δ; 1.20(s, 3H), 1.52(s, 3H), 2.66(s, 3H), 2.98-3.33(m, 4H), 4.09(m, 1H), 4.71(br s, 1H), 6.09(s, 2H), 6.33(br s, 1H), 7.23-7.34(m, 5H), 7.51(s, 1H), 7.86(s, 1H), 8.51(s, 1H)
MS(ESI$^+$)m/z; 388 [M+1]$^+$
MS(ESI$^-$)m/z; 432 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 15
(*3R*,4S**)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carboxamide



This compound was synthesized from (*3R*,4S**)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile similarly to the process of Synthesis Example 11 (yield: 9%).

White crystals

mp: 168-169°C

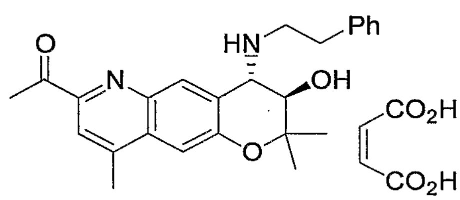
^{1}H-NMR($CDCl_3$) δ; 1.26(s, 3H), 1.57(s, 3H), 1.83(br s, 3H), 2.65(s, 2H), 2.90-3.16(m, 4H), 3.66(d, *J* = 10.2 Hz, 1H), 3.95(d, *J* = 10.5 Hz, 1H), 5.61(br s, 1H), 7.24-7.36(m, 5H), 7.85(s, 1H), 8.00(br s, 1H), 8.04(s, 1H)

MS(ESI$^+$)m/z; 406 [M+1]$^+$

MS(ESI$^-$)m/z; 450 [M+45]$^+$ (HCOOH adduct)

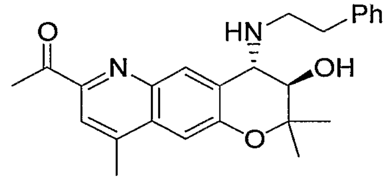
Synthesis Example 16

(*3R*,4S**)-{3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-7-yl}ethanone 1 maleate



This compound was synthesized according to the process of Synthesis Example 12.

(*3R*,4S**)-{3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-7-yl}ethanone



To a solution of (*3R*,4S**)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile (120 mg, 0.309 mmol) in benzene (1.6 mL)-diethyl ether

(1.4 mL), a solution of 3.0 M methyl magnesium bromide in diethyl ether (0.30 mL) was added dropwise at 0-5°C, and the resulting mixture was stirred for 2 hours. A solution of 3.0 M methyl magnesium bromide in diethyl ether (0.50 mL) was added dropwise at 0-5°C, and the resulting mixture was further stirred for 30 minutes. Upon the completion of the reaction, aqueous ammonium chloride solution was added and the resulting solution was extracted with ethyl acetate. The resulting organic phase was dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography and the aimed product was obtained (yield: 25%).

^{1}H-NMR($CDCl_3$) δ; 1.19(s, 3H), 1.49(s, 3H), 2.53(d, J = 0.8 Hz, 3H), 2.76(s, 3H), 2.77-3.06(m, 5H), 3.55(d, J = 10.5 Hz, 1H), 3.81(dd, J = 1.4 Hz, 10.5 Hz, 1H), 7.15-7.29(m, 6H), 7.78(s, 1H), 7.85(d, J = 1.4 Hz, 1H)

MS(ESI$^+$)m/z; 405 $[M+1]^+$

(*3R*,4S**)-{3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-yl}ethanone 1 maleate

To a solution of (*3R*,4S**)-{3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-yl}ethanone (31.3 mg, 0.077 mmol) in ethyl acetate (2 mL), a solution of maleic acid (10.0 mg, 0.086 mmol) in ethyl acetate (2 mL) was added dropwise, and precipitated solid was filtered to obtain the aimed product (yield: 80%).

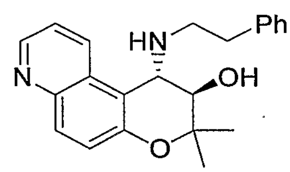
White crystals

mp: 230-234°C (decomposition)

^{1}H-NMR(DMSO-d_6) δ; 1.18(s, 3H), 1.51(s, 3H), 2.66(s, 3H), 2.74(s, 3H),2.98-3.34(m, 4H), 4.10(m, 1H), 4.66(br s, 1H), 6.05(s, 2H), 6.29(br s, 1H), 7.25-7.36(m, 5H), 7.48(s, 1H), 7.87(s, 1H), 8.56(s, 1H)

Synthesis Example 17

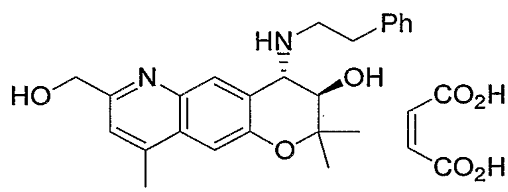
(*1S*,2R**)-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinolin-2-ol



This compound was synthesized according to the process of Synthesis

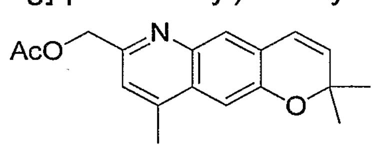
Example 12.
(Yield: 2-steps, 4%)
White crystals
mp: 170-171°C
^{1}H-NMR($CDCl_3$) δ; 1.31(s, 3H), 1.45(s, 3H), 1.61(br s, 6H), 2.71-2.84(m, 3H), 2.91-2.97(m, 1H), 3.83(d, J = 5.5 Hz, 1H), 4.11(d, J = 5.5 Hz, 1H), 7.12(d, J = 7.98 Hz, 1H), 7.18-7.25(m, 5H), 7.90(d, J = 9.1 Hz, 1H), 8.15(d, J = 8.5 Hz, 1H), 8.73(dd, J = 1.4 Hz, 4.1 Hz, 1H)
MS(ESI$^+$)m/z; 349 [M+1]$^+$
MS(ESI$^-$)m/z; 393 [M+45]$^+$ (HCOOH adduct)
Epoxy form, 97.1% ee; CHIRALCEL OJ-R acetonitrile/methanol/0.01 M aqueous sodium chloride solution = 1/3/3, Retention time: 7.0 min.

Synthesis Example 18
(*3R*,4S**)-7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



This compound was synthesized according to the process of Synthesis Example 12.

(2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinolin-7-yl)-methyl acetate



To a solution of 2,2,7,9-tetramethyl-2*H*-pyrano[2,3-g]quinoline (3.0 g, 12.5 mmol) in chloroform (30.0 mL), a solution of *m*-chloroperbenzoic acid (4.76 g, 27.6 mmol) in chloroform (12 mL)-methanol (3 mL) was added dropwise at room temperature, and the resulting mixture was stirred at room temperature for 30 minutes. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added to the reaction solution, and it was extracted. The resulting organic phase was washed with sodium hydrogencarbonate and then with aqueous sodium chloride

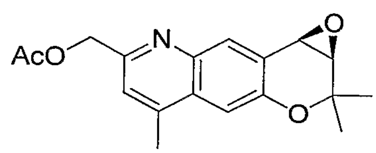
solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, acetic anhydride (12 mL) was added to the residue, and the resulting mixture was stirred at 150°C for 1 hour. Upon the completion of the reaction, acetic anhydride was distilled off, the residue was neutralized with aqueous sodium carbonate solution, extracted with chloroform, and the resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 2/1) and the aimed product was obtained (yield: 64%).

Black oily product

^{1}H-NMR($CDCl_3$) δ; 1.50(s, 6H), 2.17(s, 3H), 2.61(s, 3H), 5.30(s, 2H), 5.90(d, J = 9.91 Hz, 1H), 6.57(d, J = 9.9 Hz, 1H), 7.19(s, 1H), 7.24(s, 1H), 7.70(s, 1H)

MS(ESI$^+$)m/z; 298 [M+1]$^+$

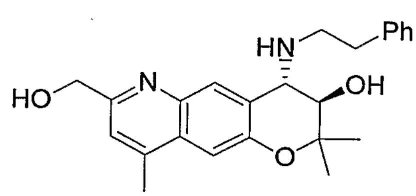
(*3R**,*4R**)-(3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-7-yl)-methy lacetate



> 99.9% ee; CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 5.4 min.

MS(ESI$^+$)m/z; 314 [M+1]$^+$

(*3R**,*4S**)-7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-py rano[2,3-g]quinolin-3-ol



To a solution of (*3R**,*4R**)-(3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-7-yl)-methy l acetate (403 mg, 1.29 mmol) in 1,4-dioxane (1 mL), lithium perchlorate (137 mg, 1.29 mmol) and 2-phenylethylamine (0.195 mL, 1.55 mmol) were added at room temperature and the resulting mixture was stirred at 70°C for 1.5 hour. Upon the

completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and it was extracted with ethyl acetate. The resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 1/1) and the aimed product was obtained (yield: 32%).

^{1}H-NMR($CDCl_3$) δ; 1.24(s, 3H), 1.55(s, 3H), 2.58(s, 3H), 2.87-3.08(m, 5H), 3.63(d, *J* = 10.2 Hz, 1H), 3.81(d, *J* = 10.5 Hz, 1H), 4.82(s, 2H), 7.02(s, 1H), 7.23-7.36(m, 6H), 7.75(s, 1H)

MS(ESI$^+$)m/z; 393 [M+1]$^+$

MS(ESI$^-$)m/z; 437 [M+45]$^+$ (HCOOH adduct)

(*3R*,4S**)-7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate

To a solution of (*3R*,4S**)-7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol (157 mg, 0.407 mmol) in ethyl acetate (4 mL), a solution of maleic acid (52 mg, 0.448 mmol) in ethyl acetate (2mL) was added dropwise, and precipitated solid was filtered to obtain the aimed compound (yield: 80%).

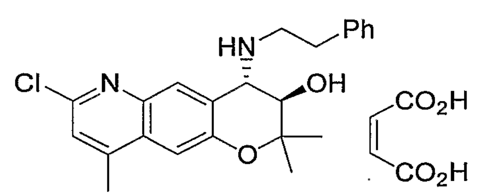
Pale yellow crystals

mp: 216-221°C

^{1}H-NMR(DMSO-d_6) δ; 1.17(s, 3H), 1.50(s, 3H), 2.60(s, 3H), 2.98-3.40(m, 4H), 4.06-4.11(m, 1H), 3.81(d, *J* = 10.5 Hz, 1H), 4.66-4.69(3H), 5.50(br s, 1H), 6.06(s, 2H), 6.30(br s, 1H), 7.23-7.35(m, 5H), 7.40(s, 1H), 7.47(s, 1H), 8.35(s, 1H)

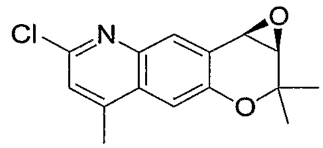
Synthesis Example 19

(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



This compound was synthesized according to the process of Synthesis Example 12.

(*3R*, 4R**)-7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline

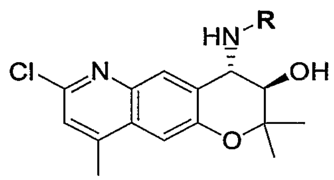


(Yield: 78%)
97.1% ee; CHIRALCEL OJ-R acetonitrile/methanol/0.01 M aqueous sodium chloride solution = 1/3/3, Retention time: 18.9 min.
Yellow amorphous product
^{1}H-NMR($CDCl_3$) δ; 1.28(s, 3H), 1.65(s, 3H), 2.59(d, J = 0.8 Hz, 3H), 3.60(d, J = 4.4 Hz, 1H), 4.13(d, J = 4.4 Hz, 1H), 7.19(s, 1H), 7.29(d, 1H), 8.02(s, 1H)
MS(ESI$^+$)m/z; 276 [M+1]$^+$

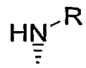
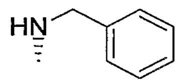
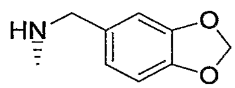
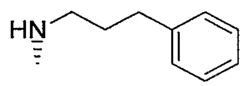
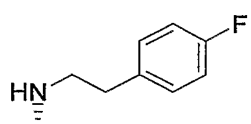
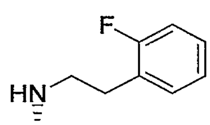
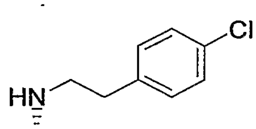
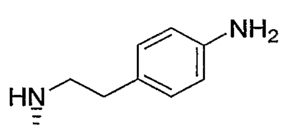
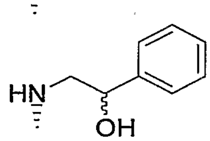
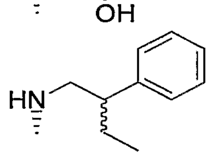
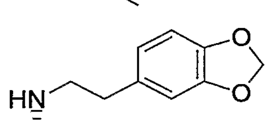
(*3R*, 4S**)-7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate
(2-steps, yield: 34%)

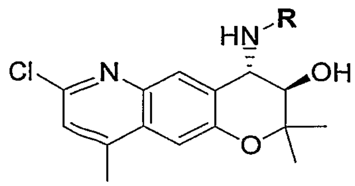
Synthesis Examples 20-49

Synthesis Examples 20-49 were carried out similarly to the process of Synthesis Example 19.

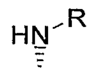
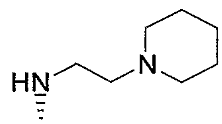
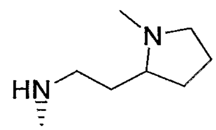
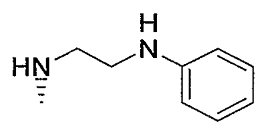
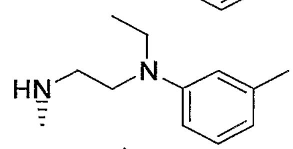
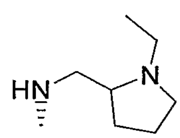
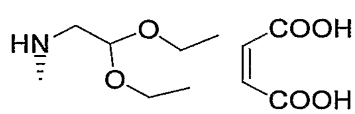


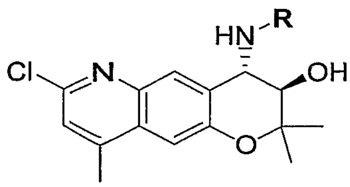
optically active

Compound No.	
Synthesis Example 20	
Synthesis Example 21	
Synthesis Example 22	
Synthesis Example 23	
Synthesis Example 24	
Synthesis Example 25	
Synthesis Example 26	
Synthesis Example 27	
Synthesis Example 28	
Synthesis Example 29	

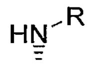
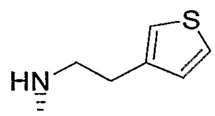
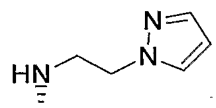
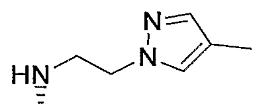
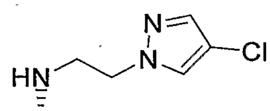
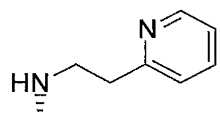
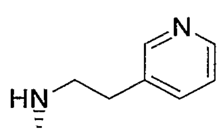
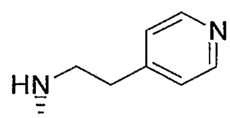


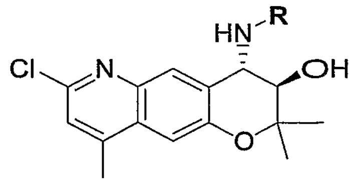
optically active

Compound No.	
Synthesis Example 30	
Synthesis Example 31	
Synthesis Example 32	
Synthesis Example 33	
Synthesis Example 34	
Synthesis Example 35	

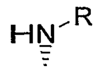
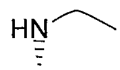
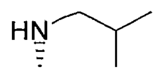
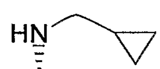
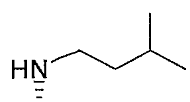
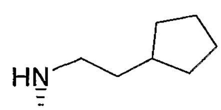
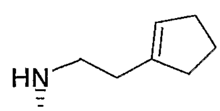
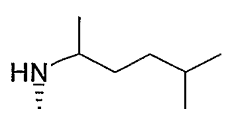


optically active

Compound No.	
Synthesis Example 36	
Synthesis Example 37	
Synthesis Example 38	
Synthesis Example 39	
Synthesis Example 40	
Synthesis Example 41	
Synthesis Example 42	



optically active

Compound No.	
Synthesis Example 43	
Synthesis Example 44	
Synthesis Example 45	
Synthesis Example 46	
Synthesis Example 47	
Synthesis Example 48	
Synthesis Example 49	

Synthesis Example 20

(*3R*,4S**)-4-(benzylamino)-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 81%)

Colorless amorphous product

^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.58 (s, 3H), 1.60 (br s, 1H), 2.60 (s, 3H), 3.12 (s,

1H), 3.72 (d, J = 10.3 Hz, 1H), 3.91 (d, J = 10.3 Hz, 1H), 3.85-4.00 (m, 2H), 7.17 (s, 1H), 7.30-7.40 (m, 6H), 8.08 (s, 1H).
MS (ESI$^+$) m / z; 383 [M+1]$^+$
MS (ESI$^-$) m / z; 427[M+45]$^+$ (HCOOH adduct)

Synthesis Example 21
(*3R*,4S**)-4-{[((1,3-benzodioxol-5-yl)methyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 92%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.57 (s, 3H), 2.59 (s, 3H), 3.70 (d, J = 10.3 Hz, 1H), 3.82 (ABq, J = 12.8 Hz, 2H), 3.97 (dd, J = 10.3, 1.2 Hz, 1H), 5.96 (s, 2H), 6.77 (d, J = 8.0 Hz, 1H), 6.82 (dd, J = 8.0, 1.6 Hz, 1H), 6.89 (d, J = 1.6 Hz, 1H), 7.13 (s, 1H), 7.30 (s, 1H), 8.04 (s, 1H)
MS (ESI$^+$) m / z; 427 [M+1]$^+$

Synthesis Example 22
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-[(3-phenylpropyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 72%)
Colorless amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.57 (s, 3H), 1.80-1.95 (m, 2H), 2.59 (s, 3H), 2.65-2.85 (m, 5H), 3.24 (s, 1H), 3.61 (d, J = 10.4 Hz, 1H), 3.86 (d, J = 10.4 Hz, 1H), 7.10-7.20 (m, 3H), 7.25-7.35 (m, 3H), 7.94 (s, 1H).
MS (ESI$^+$) m / z; 411 [M+1]$^+$
MS (ESI$^-$) m / z; 455 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 23
(*3R*,4S**)-7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 96%)
Colorless amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.25 (s, 3H), 1.55 (s, 3H), 1.57 (br s, 1H), 2.58 (s, 3H), 2.80 (t, J = 6.9 Hz, 2H), 2.90-3.10 (m, 3H), 3.58 (d, J = 10.4 Hz, 1H), 3.86 (d, J = 10.4 Hz, 1H), 6.95-7.05 (m, 2H), 7.15-7.20 (m, 3H), 7.26 (s, 1H), 7.89 (s, 1H).

MS (ESI$^+$) m / z; 415 $[M+1]^+$

Synthesis Example 24

(*3R*,4S**)-7-chloro-4-{[2-(2-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 79%)

Colorless amorphous product

^{1}H-NMR ($CDCl_3$) δ: 1.25 (s, 3H), 1.54 (s, 3H), 1.61 (br s, 1H), 2.57 (s, 3H), 2.86 (t, *J* = 6.9 Hz, 2H), 2.95-3.10 (m, 3H), 3.56 (d, *J* = 10.4 Hz, 1H), 3.85 (d, *J* = 10.4 Hz, 1H), 7.00-7.25 (m, 6H), 7.90 (s, 1H).

MS (ESI$^+$) m / z; 415 $[M+1]^+$

Synthesis Example 25

(*3R*,4S**)-7-chloro-4-{[2-(4-chlorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 78%)

Colorless amorphous product

Synthesis Example 26

(*3R*,4S**)-4-{[2-(4-aminophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 40%)

Colorless amorphous product

^{1}H-NMR ($CDCl_3$) δ: 1.23 (s, 3H), 1.55 (s, 3H), 1.58 (br s, 3H), 2.57 (s, 3H), 2.71 (t, *J* = 7.4 Hz, 2H), 2.85-3.05 (m, 2H), 3.11 (br s, 1H), 3.57 (d, *J* = 10.4 Hz, 1H), 3.84 (d, *J* = 10.4 Hz, 1H), 6.65 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 8.5 Hz, 2H), 7.11 (s, 1H), 7.25 (s, 1H), 7.81 (s, 1H).

MS (ESI$^+$) m / z; 412 $[M+1]^+$

MS (ESI$^-$) m / z; 456 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 27

(*3R*,4S**)-7-chloro-4-[(2-hydroxy-2-phenylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 72%)

Colorless amorphous product

^{1}H-NMR ($CDCl_3$) δ: 1.27 (s, 1.5H), 1.28 (s, 1.5H), 1.56 (s, 3H), 1.77(br s, 2H), 2.57 (s, 3H), 2.85-3.15 (m, 2H), 3.68 (d, *J* = 10.2 Hz, 1H), 3.75 (d, *J* = 10.2 Hz, 1H), 4.75-4.85 (m, 1H), 7.25 (s, 1H), 7.27-7.40 (s, 6H), 7.99 (s, 0.5H), 8.00 (s, 0.5H).
MS (ESI$^+$) m / z; 413[M+1]$^+$
MS (ESI$^-$) m / z; 457[M+45]$^+$ (HCOOH adduct)

Synthesis Example 28
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-[(2-phenylbutyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 50%)
Pale brown amorphous product
^{1}H-NMR ($CDCl_3$) δ: 0.86 (t, *J* = 7.3 Hz, 3H), 1.20 (s, 3H), 1.53 (s, 3H), 1.51-1.71 (m, 2H), 2.57 (s, 3H), 2.57-2.64 (m, 1H), 2.86 (dd, *J* = 11.6, 9.1 Hz, 1H), 2.86 (dd, *J* = 11.6, 5.2 Hz, 1H), 3.55 (d, *J* = 10.2 Hz, 1H), 3.74 (d, *J* = 10.2 Hz, 1H), 7.15 (s, 1H), 7.20-7.32 (m, 4H), 7.35-7.41 (m, 2H), 7.74 (s, 1H)
MS (ESI$^+$) m / z; 425 [M+1]$^+$

Synthesis Example 29
(*3R*,4S**)-4-{[2-(1,3-benzodioxol-5-yl)ethyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 62%)
Pale brown amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.26 (s, 3H), 1.56 (s, 3H), 1.66 (br, 1H), 2.57 (s, 3H), 2.74 (t, *J* = 6.9 Hz, 2H), 2.89-3.00 (m, 2H), 3.1 (br, 1H), 3.60 (d, *J* = 10.4 Hz, 1H), 3.86 (d, *J* = 10.4 Hz, 1H), 5.95 (ABq, 2H), 6.66-6.77 (m, 3H), 7.15 (s, 1H), 7.26 (s, 1H), 7.83 (s, 1H)
MS (ESI$^+$) m / z; 441 [M+1]$^+$

Synthesis Example 30
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[2-(1-piperidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 61%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.29 (s, 3H), 1.58 (s, 3H), 1.60 (br s, 2H), 1.50-1.70 (m, 6H), 2.30-2.60 (m, 6H), 2,58 (s, 3H), 3.06 (t, *J* = 5.8 Hz, 2H), 3.54 (d, *J* = 10.4 Hz, 1H),

3.80 (d, J = 10.4 Hz, 1H), 7.13 (s, 1H), 7.23 (s, 1H), 8.06 (s, 1H).
MS (ESI^+) m / z; 404 $[M+1]^+$
MS (ESI^-) m / z; 448 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 31
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[2-(1-methyl-2-pyrrolidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 55%)
Colorless amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.29 (s, 3H), 1.58 (s, 3H), 1.49-2.00 (m ,8H), 2.10-2.25 (m, 2H), 2.34 (s, 1.5H), 2.35 (s, 1.5H), 2.58 (s, 3H), 2.65-2.85 (m, 2H), 3.00-3.15 (m, 1H), 3.62 (d, J = 10.4 Hz, 0.5H), 3.70 (d, J = 10.4 Hz, 0.5H), 3.85 (d, J = 10.4 Hz, 0.5H), 3.88 (d, J = 10.4 Hz, 0.5H), 7.15 (s, 1H), 7.27 (s, 1H), 7.96 (s, 1H).
MS (ESI^+) m / z; 404 $[M+1]^+$
MS (ESI^-) m / z; 448 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 32
(*3R*,4S**)-4-[(2-anilinoethyl)amino]-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 78%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.27 (s, 3H), 1.56 (s, 3H), 1.77 (br s, 3H), 2.58 (s, 3H), 2.95-3.10 (m, 2H), 3.30 (t, J = 5.5 Hz, 2H), 3.64 (d, J = 10.2 Hz, 1H), 3.93 (d, J= 10.2 Hz, 1H), 6.65-6.80 (m, 3H), 7.15-7.20 (m, 3H), 7.28 (s, 1H), 7.98 (s, 1H).
MS (ESI^+) m / z; 412 $[M+1]^+$
MS (ESI^-) m / z; 456 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 33
(*3R*,4S**)-7-chloro-4-({2-[ethyl(3-methylphenyl)amino]ethyl}amino)-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 90%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.23 (t, J = 6.9 Hz, 3H), 1.26 (s, 3H), 1.55 (s, 3H), 1.62 (br s, 1H), 2.27 (s, 3H), 2.57 (s, 3H), 2.80-3.00 (m, 2H), 3.30-3.50 (m, 5H), 3.61 (d, J = 10.1 Hz, 1H), 3.91 (d, J = 10.1 Hz, 1H), 6.60-6.70 (m, 4H), 7.05-7.15 (m, 2H), 7.96 (s, 1H).

MS (ESI^+) m / z; 454 $[M+1]^+$
MS (ESI^-) m / z; 498 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 34
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[(1-ethyl-(R)-2-pyrrolidinyl)methyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 93%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.27 (s, 1H), 1.32 (t, *J* = 7.1 Hz, 2H), 1.56 (s, 3H), 1.95-2.12 (br, 4H),2.56 (s, 3H), 2.71-2.81 (br, 2H), 2.98-3.37 (m, 4H), 3.64-4.01 (m, 5H), 7.12 (s, 1H), 7.22 (s, 1H), 8.01 (s, 1H)
MS (ESI^+) m / z; 405 $[M+1]^+$
MS (ESI^-) m / z; 448 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 35
(*3R*,4S**)-7-chloro-4-[(2,2-diethoxyethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol maleate
(Yield: 88%)
White solid
^{1}H-NMR (CD_3OD) δ: 1.23-1.30 (m, 9H), 1.57 (s, 3H), 2.64 (s, 3H), 3.50-3.85 (m, 4H), 4.02 (d, *J* = 10.2 Hz, 1H), 6.27 (s, 1H), 7.37 (s, 1H), 7.49 (s, 1H), 8.13 (s, 1H)
Free form
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-[(2,2-diethoxyethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
Pale yellow amorphous product
MS (ESI^+) m / z; 410 $[M+1]^+$
MS (ESI^-) m / z; 453 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 36
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[2-(3-thienyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 57%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.24 (s, 3H), 1.55 (s, 3H), 2.56 (s, 3H), 2.84 (t, *J* = 6.8 Hz, 2H), 2.90-3.09 (m, 2H), 3.60 (d, *J* = 10.5 Hz, 1H), 3.86 (d, *J* = 10.5 Hz, 1H), 6.94-7.01 (m,

2H), 7.13 (s, 1H), 7.24-7.29 (m, 2H), 7.89 (s, 1H)
MS (ESI^+) m / z; 404 $[M+1]^+$
MS (ESI^-) m / z; 447 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 37
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-[2-(1-pyrazolylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 59%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.58 (s, 3H), 1.86 (br s, 1H), 2.57 (s, 3H), 3.26-3.31 (m, 2H), 3.63 (d, *J* = 10.1 Hz, 1H), 3.87 (d, *J* = 10.1 Hz, 1H), 4.24-4.32 (m, 2H), 5.00 (br s, 1H), 6.32 (dd, *J* = 1.7, 3.4 Hz, 1H), 7.14 (s, 1H), 7.25 (s, 1H), 7.45 (d, *J* = 1.7 Hz, 1H), 7.58 (d, *J* = 1.7 Hz, 1H), 8.00 (s, 1H)
MS (ESI^+) m / z; 387 $[M+1]^+$

Synthesis Example 38
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[2-(4-methylpyrazol-1-yl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 70%)
Colorless amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.58 (s, 3H), 2.00 (br s, 1H), 2.10 (s, 3H), 2.57 (s, 3H), 3.16-3.31 (m, 2H), 3.64 (d, *J* = 10.2 Hz, 1H), 3.87 (d, *J* = 10.2 Hz, 1H), 4.11-4.30 (m, 2H), 5.20 (br s, 1H), 7.13 (s, 1H), 7.21 (s, 1H), 7.24 (s, 1H), 7.36 (s, 1H), 7.98 (s, 1H)
MS (ESI^+) m / z; 401 $[M+1]^+$

Synthesis Example 39
(*3R*,4S**)-7-chloro-4-{[2-(4-chloropyrazol-1-yl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 89%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.58 (s, 3H), 1.84 (br s, 1H), 2.58 (s, 3H), 3.26-3.29 (m, 2H), 3.61 (d, *J* = 10.4 Hz, 1H), 3.87 (d, *J* = 10.4 Hz, 1H), 4.16-4.29 (m, 2H), 4.51 (br s, 1H), 7.15 (s, 1H), 7.26 (s, 1H), 7.45 (s, 1H), 7.48 (s, 1H), 7.97 (s, 1H)
MS (ESI^+) m / z; 421 $[M+1]^+$

Synthesis Example 40
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[2-(2-pyridy)lethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 83%)
Yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.32 (s, 3H), 1.61 (s, 3H), 1.82 (br s, 1H), 2.57 (s, 3H), 2.92-3.12 (m, 2H), 3.26-3.30 (m, 2H), 3.74 (d, *J* = 10.2 Hz, 1H), 3.92 (d, *J* = 10.2 Hz, 1H), 7.13 (s, 1H), 7.17-7.27 (m, 3H), 7.64-7.70 (m, 1H), 8.06 (s, 1H), 8.56 (d, *J* = 5.0 Hz, 1H)
MS (ESI$^+$) m / z; 398 $[M+1]^+$

Synthesis Example 41
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[2-(3-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 61%)
Brown amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.26 (s, 3H), 1.55 (s, 3H), 1.73 (br s, 1H), 2.58 (s, 3H), 2.80-2.85 (m, 2H), 2.92-3.07 (m, 2H), 3.23 (br s, 1H), 3.61 (d, *J* = 10.4 Hz, 1H), 3.89 (d, *J* = 10.4 Hz, 1H), 7.16 (s, 1H), 7.22-7.27 (m, 2H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.93 (s, 1H), 8.47-8.48 (m, 2H)
MS (ESI$^+$) m / z; 398 $[M+1]^+$

Synthesis Example 42
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[2-(4-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 47%)
Pale brown amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.26 (s, 3H), 1.55 (s, 3H), 1.89 (br s, 1H), 2.58 (s, 3H), 2.80-2.85 (m, 2H), 2.94-3.11 (m, 2H), 3.60 (br s, 1H)), 3.63 (d, *J* = 10.4 Hz, 1H), 3.90 (d, *J* = 10.4 Hz, 1H), 7.15 (d, *J* = 5.7 Hz, 1H), 7.16 (s, 1H), 7.27 (s, 1H), 7.96 (s, 1H), 8.47 (d, *J* = 5.7 Hz, 2H)
MS (ESI$^+$) m / z; 398 $[M+1]^+$

Synthesis Example 43
(*3R*,4S**)-7-chloro-4-ethylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-

3-ol
(Yield: 95%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.18 (t, J = 7.1 Hz, 3H), 1.29 (s, 3H), 1.58 (s, 3H), 2.58 (s, 3H), 2.68-2.91 (m, 2H), 3.63 (d, J = 10.4 Hz, 1H), 3.87 (dd, J =10.4, 1.2 Hz, 1H), 7.15 (d, J = 1.1 Hz, 1H), 7.27 (s, 1H), 7.93 (d, J = 1.1 Hz, 1H).
MS (ESI$^+$) m / z; 321 [M+1]$^+$

Synthesis Example 44
(*3R*,4S**)-7-chloro-4-isobutylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 96%)
Pale brown amorphous product
^{1}H-NMR ($CDCl_3$) δ: 0.94-0.98 (m, 6H), 1.29 (s, 3H), 1.58 (s, 3H), 1.68-1.76 (m, 1H), 2.50-2.62 (m, 2H), 2.58 (s, 3H), 3.36 (br s, 1H), 3.63 (d, J = 10.2 Hz, 1H), 3.88 (dd, J = 10.2, 1.1 Hz, 1H), 7.15 (s, 1H), 7.28 (s, 1H), 7.93 (s, 1H)
MS (ESI$^+$) m / z; 239 [M+1]$^+$

Synthesis Example 45
(*3R*,4S**)-7-chloro-4-[(cyclopropylmethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 85%)
Pale brown amorphous product
^{1}H-NMR ($CDCl_3$) δ: 0.13-0.20 (m, 2H), 0.48-0.54 (m, 2H), 0.95-1.01 (m, 1H), 1.29 (s, 3H), 1.58 (s, 3H), 1.8 (br s, 1H), 2.53 (m, 1H), 2.58 (s, 3H), 2.70 (m, 1H), 3.63 (d, J = 10.4 Hz, 1H), 3.91 (d, J = 10.4 Hz, 1H), 7.15 (s, 1H), 7.27 (s, 1H), 7.90 (s, 1H)
MS (ESI$^+$) m / z; 347 [M+1]$^+$

Synthesis Example 46
(*3R*,4S**)-7-chloro-4-isopentylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 64%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 0.90 (d, 6H), 1.29 (s, 3H), 1.39-1.46 (m, 2H), 1.58 (s, 3H), 1.62-1.74 (m, 2H), 2.58 (s, 3H), 2.64-2.85 (m, 2H), 3.64 (d, J = 10.4 Hz, 1H), 3.87 (d,

J = 10.4 Hz, 1H), 7.15 (s, 1H), 7.28 (s, 1H), 7.93 (s, 1H)
MS (ESI$^+$) m / z; 363 [M+1]$^+$

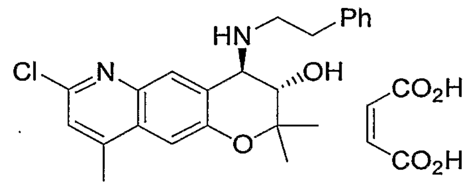
Synthesis Example 47
(*3R*,4S**)-7-chloro-4-[2-(cyclopentylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 78%)
Pale yellow solid
^{1}H-NMR ($CDCl_3$) δ: 1.08-1.11 (m, 2H), 1.29 (s, 3H), 1.49-1.62 (m, 6H), 1.54 (s, 3H), 1.71-1.83 (m, 3H), 2.58 (s, 3H), 2.67-2.82 (m, 2H), 3.63 (d, J = 10.4 Hz, 1H), 3.86 (d, J = 10.4 Hz, 1H), 7.15 (s, 1H), 7.27 (s, 1H), 7.93 (s, 1H)
MS (ESI$^+$) m / z; 389 [M+1]$^+$

Synthesis Example 48
(*3R*,4S**)-7-chloro-4-{[2-(1-cyclopentenyl)ethyl]amino]}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 70%)
Pale brown amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.58 (s, 3H), 1.86-1.94 (m, 2H), 2.22-2.34 (m, 7H), 2.58 (s, 3H), 2.79-2.96 (m, 2H), 3.63 (d, J = 10.5 Hz, 1H), 3.87 (dd, J = 10.5, 1.2 Hz, 1H), 5.44 (s, 1H), 7.15 (s, 1H), 7.27 (s, 1H), 7.92 (s, 1H)
MS (ESI$^+$) m / z; 387 [M+1]$^+$

Synthesis Example 49
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-[(5-methylhexane-2-yl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 83%)
Pale yellow amorphous product
^{1}H-NMR ($CDCl_3$) δ: 0.91 (dd, J = 6.6 Hz, 9.6Hz,6H), 1.13-1.34 (m, 9H), 1.56 (s, 6H), 2.57 (s, 3H), 3.22-3.44 (m, 2H), 3.80-3.85 (br s, 1H), 7.14 (s, 1H), 7.26 (s, 1H), 7.96-7.98 (br s, 1H)
MS (ESI$^+$) m / z; 392 [M+2]$^+$
MS (ESI$^-$) m / z; 435 [M+45]$^+$ (HCOOH adduct)

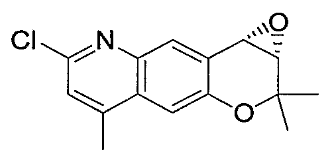
Synthesis Example 50

(*3S*,4R**)-7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



This compound was synthesized by using the enantiomer of Ph,Ph salen manganese complex (XX) (hereinafter, referred to as ent-Ph,Ph salen manganese complex).

(*3S*,4S**)-7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline



To a solution of 7-chloro-2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline (200 mg, 0.77 mmol) in ethyl acetate (3.0 mL), *N*-methyl imidazole (0.012 mL, 0.154 mmol) and ent-Ph,Ph salen manganese complex (8.0 mg, 0.0077 mmol) were added at room temperature and aqueous sodium hypochlorite solution (1.0 g, 1.513 mol/kg, 1.54 mmol) was added dropwise, and the resulting mixture was stirred for 40 minutes. Aqueous sodium hypochlorite solution (1.0 g, 1.513 mol/kg, 1.54 mmol) was added dropwise, and the resulting mixture was further stirred at room temperature for 30 minutes. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added to the reaction solution, the resulting solution was filtered through celite and extracted. The organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 10/1) to obtain (*3S*,4S**)-7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline (yield: 94%).

> 99.9% ee; CHIRALCEL OJ-R acetonitrile/methanol/0.01 M aqueous sodium chloride solution = 1/3/3, Retention time: 44.3 min.

(*3S*,4R**)-7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3

-g]quinolin-3-ol 1 maleate

To a solution of (*3S*,4S**)-7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline (199 mg, 0.72 mmol) in 1,4-dioxane (0.4 mL), lithium perchlorate (77.0 mg, 0.72 mmol) and 2-phenylethylamine (0.11 mL, 0.87 mmol) were added at room temperature and the resulting mixture was stirred at 70°C for 3 hours. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and it was extracted with ethyl acetate and the resulting organic phase was washed with aqueous sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 3/1). Further, after distilling off the solvent, ethyl acetate (2 mL) was added and a solution of maleic acid (50.3 mg, 0.43 mmol) in ethyl acetate (2mL) was added dropwise. The precipitated solid was filtered to obtain (*3S*,4R**)-7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate (yield: 41%).

White crystals

mp: 240-242°C

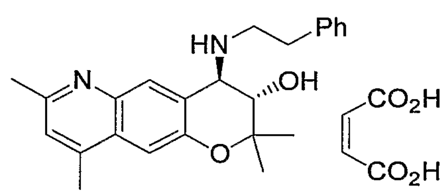
^{1}H-NMR(DMSO-d_6): 1.18(s, 3H), 1.50(s, 3H), 2.60(s, 3H), 2.97-3.32(m, 4H), 4.04-4.09(m, 1H), 4.65(d, *J* = 9.6 Hz, 1H), 6.05(s, 2H), 6.29(br s, 1H), 7.23-7.35(m, 5H), 7.44(s, 2H), 8.32(s, 1H)

MS(ESI$^+$)m/z; 397 [M+1]$^+$

MS(ESI$^-$)m/z; 441 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 51

(*3S*,4R**)-2,2,7,9-tetramethyl-4-[(2-pentylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



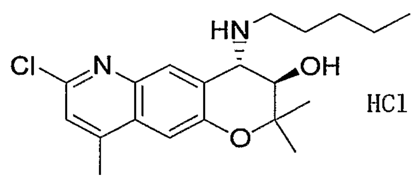
This compound was synthesized according to the process of Synthesis Example 50.

(2-steps yield: 25%)

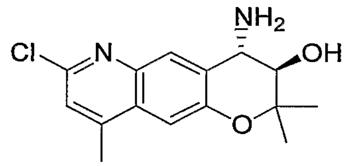
epoxy 99.1%ee CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile =

60/40, Retention time: 10.3 min.
White crystals
mp: 215-216°C (decomposition)
^{1}H-NMR(DMSO-d_6); 1.16(s, 3H), 1.49(s, 3H), 2.55(s, 3H), 2.58(s, 3H), 2.97-3.32 (m, 4H), 4.02-4.04(m, 1H), 4.62(br s, 1H), 6.04(s, 2H), 6.25(br s, 1H), 7.24-7.36(m, 7H), 8.31(s, 1H)
MS(ESI$^+$)m/z; 377 [M+1]$^+$

Synthesis Example 52
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride



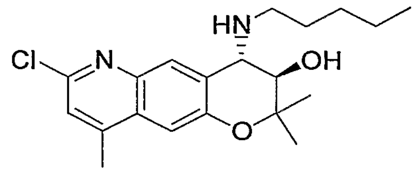
(*3R*,4S**)-4-amino-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



To a solution of (*3R*,4R**)-7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline (2.0 g, 7.25 mmol) in ethanol (20 mL), ammonia water (10 mL) was added, and the resulting mixture was stirred in a sealed tube at 90°C for 3 hours. Upon the completion of the reaction, the reaction solution was concentrated, and ethyl acetate was added thereto, The resulting solution was washed with water and then with saturated sodium chloride solution, and dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/2) to obtain the aimed product (yield: 86%).
White crystals
^{1}H-NMR($CDCl_3$) δ; 1.30 (s, 3H), 1.58 (s, 3H), 1.67 (br s, 2H), 2.59 (s, 3H), 3.28 (br s, 1H), 3.45 (d, J = 10.4 Hz, 1H), 3.85 (d, J = 10.4 Hz, 1H), 7.15 (s, 1H), 7.26 (s, 1H), 8.02 (s, 1H).

(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin

-3-ol



To a solution of (*3R*,4S**)-4-amino-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol (60 mg, 0.205 mmol) in methanol (1.2 mL), butyl aldehyde (35 mg, 0.041 mmol) was added, and the resulting mixture was stirred at room temperature for 20 minutes. Sodium cyanoborohydride (52 mg, 0.82 mmol) was added thereto, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, and the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, and dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 3/1) to obtain the aimed product (yield: 41%).

Colorless amorphous product

^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, *J* = 6.9 Hz, 3H), 1.29 (s, 3H), 1.20-1.45 (m, 4H), 1.55-1.70 (m, 4H), 2.58 (s, 3H), 2.60-2.82 (m, 2H), 3.63 (d, *J* = 10.4 Hz, 1H), 3.86 (d, *J* =10.4 Hz, 1H), 7.15 (s, 1H), 7.28 (s, 1H), 7.93 (s, 1H).

MS (ESI$^+$) m / z; 363 $[M+1]^+$

MS (ESI$^-$) m / z; 407 $[M+45]^+$ (HCOOH adduct)

(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin -3-ol hydrochloride

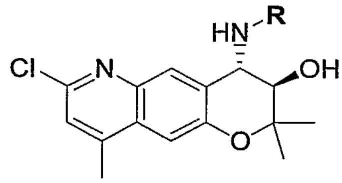
To a solution of (*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin -3-ol (28 mg, 0.77 mmol) in ether (560 μL), 4 M hydrogen chloride solution in ether (56 μL) was added dropwise, and the resulting mixture was stirred at 0°C for 15 minutes. Solid product was filtered off, washed with ether and dried to obtain the aimed product (yield: 88%).

Colorless crystals

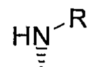
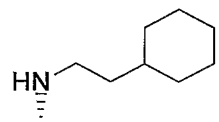
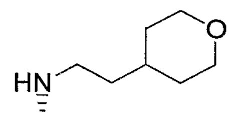
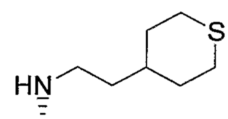
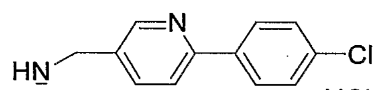
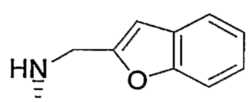
mp: 291-294°C (decomposition)

Synthesis Examples 53-57

The compounds of Synthesis Examples 53-57 were synthesized according to the process of Synthesis Example 52.



optically active

Compound No.		
Synthesis Example 53		HCl
Synthesis Example 54		HCl
Synthesis Example 55		
Synthesis Example 56		HCl
Synthesis Example 57		

Synthesis Example 53

(*3R*,4S**)-7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano [2,3-g]quinolin-3-ol hydrochloride

Free form

(*3R*,4S**)-7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano [2,3-g]quinolin-3-ol

(Yield: 31%)

Colorless amorphous product

^{1}H-NMR ($CDCl_3$) δ: 0.90-1.00 (m, 2H), 1.05-1.25 (m, 6H), 1.29 (s, 3H), 1.58 (s, 3H)1.60-1.70 (m, 7H), 2.58 (s, 3H), 2.75-2.85 (m, 2H), 3.63 (d, *J* = 10.4 Hz, 1H), 3.86 (d, *J* = 10.4 Hz, 1H), 7.15 (s, 1H), 7.27 (s, 1H), 7.93 (s, 1H)

Hydrochloride
(*3R*,4S**)-7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride
(Yield: 76%)
Colorless crystals
mp: 294-295°C (decomposition)
MS (ESI^+) m / z; 403 $[M+1]^+$
MS (ESI^-) m / z; 447 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 54
(*3R*,4S**)-7-chloro-4-[{2-(tetrahydropyran-4-yl)ethyl}amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride
Free form
(*3R*,4S**)-7-chloro-4-[{2-(tetrahydropyran-4-yl)ethyl}amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 65%)
Colorless amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.29 (s, 3H), 1.20-1.40 (m, 4H), 1.58 (s, 3H), 1.50-1.80 (m, 4H), 2.59 (s, 3H), 2.65-2.90 (s, 2H), 3.20-3.40 (m, 3H), 3.64 (d, *J* = 10.4 Hz, 1H), 3.70-3.75 (m, 1H), 3.85 (d, *J* = 10.4 Hz, 1H), 3.80-4.00 (m, 3H), 7.16 (s, 1H), 7.28 (s, 1H), 7.92 (s, 1H).
MS (ESI^+) m / z; 405 $[M+1]^+$
MS (ESI^-) m / z; 449 $[M+45]^+$ (HCOOH adduct)
Hydrochloride
(*3R*,4S**)-7-chloro-4-[{2-(tetrahydropyran-4-yl)ethyl}amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride
(Yield: 72%)
Colorless crystals
mp: 318-320°C (decomposition)

Synthesis Example 55
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-[{2-(4-thianyl)ethyl}amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 63%)
Colorless amorphous product

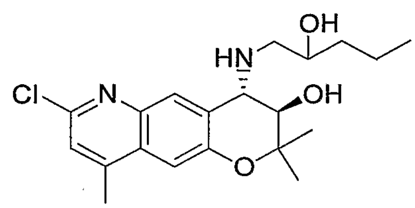
^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.40-1.60 (m, 5H), 1.56 (s, 1H), 1.90-2.00 (m, 2H), 2.59 (s, 3H), 2.50-2.85 (m, 6H), 3.23 (s, 1H), 3.63 (d, *J* = 10.4 Hz, 1H), 3.87 (d, *J* = 10.4 Hz, 1H), 7.16 (s, 1H), 7.28 (s, 1H), 7.91 (s, 1H).
MS (ESI^+) m / z; 421 $[M+1]^+$
MS (ESI^-) m / z; 465 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 56
(*3R*,4S**)-7-chloro-4-({[6-(4-chlorophenyl)-3-pyridinyl]methyl}amino)-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride
Free form
(*3R*,4S**)-7-chloro-4-({[6-(4-chlorophenyl)-3-pyridinyl]methyl}amino)-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 16%)
^{1}H-NMR ($CDCl_3$) δ: 1.30 (s, 3H), 1.59 (s, 3H), 1.60 (br s, 1H), 2.60 (s, 3H), 2.98 (s, 1H), 3.75-4.10 (m, 4H), 7.19 (s, 1H), 7.34 (s, 1H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 9.0 Hz, 1H), 7.80 (dd, *J* = 9.0, 2.2Hz, 1H), 7.96 (d, *J* =8.8 Hz, 2H), 8.09 (s, 1H), 8.66 (d, *J* = 2.2 Hz, 1H).
MS (ESI^+) m / z; 494$[M+1]^+$
MS (ESI^-) m / z; 538 $[M+45]^+$ (HCOOH adduct)
Hydrochloride
(*3R*,4S**)-7-chloro-4-({[6-(4-chlorophenyl)-3-pyridinyl]methyl}amino)-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride
(Yield: 67%)
Pale yellow solid

Synthesis Example 57
(*3R*,4S**)-4-[(2-benzofurylmethyl)amino]-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol
(Yield: 74%)
Colorless amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.58 (s, 3H), 2.0 (br), 2.59 (s, 3H), 3.35 (br, 1H), 3.75 (d, *J* = 10.2 Hz, 1H), 4.04 (dd, *J* = 10.2, 1.1 Hz, 1H), 4.06 (s, 2H), 6.60 (s, 1H), 7.16 (s, 1H), 7.18-7.27 (m, 2H), 7.30 (s, 1H), 7.46 (d, *J* = 8.3 Hz, 1H), 7.49-7.52 (m, 1H), 8.08 (d, *J* = 1.1 Hz, 1H)
MS (ESI^+) m / z; 423 $[M+1]^+$

Synthesis Example 58

(*3R*,4S**)-7-chloro-4-[(2-hydroxypentyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



Under nitrogen stream, 1,2-epoxypentane (71 μL, 0.682 mmol) was added to a solution of (*3R*,4S**)-4-amino-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol (100 mg, 0.343 mmol) and lithium perchlorate (36 mg, 0.343 mmol) in dioxane (0.50 mL) at room temperature, and the resulting mixture was stirred at 70°C for 25 hours. Upon the completion of the reaction, ethyl acetate was added thereto, the resulting reaction solution was washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated aqueous sodium chloride solution, and then dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/1) to obtain the aimed product (yield: 59%).

Pale yellow amorphous product

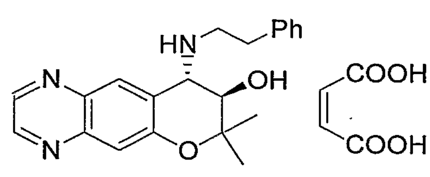
^{1}H-NMR ($CDCl_3$) δ: 0.93 (t, *J* = 6.9 Hz, 3H), 1.28 (s, 3H), 1.30-1.50 (m, 4H), 1.57 (s, 3H), 1.91 (br s, 3H), 2.59 (s, 3H), 2.60-2.70 (m, 1H), 2.85-3.00 (m, 1H), 3.60-3.75 (m, 2H), 3.90-4.00 (m, 1H), 7.16 (s, 1H), 7.28 (s, 1H), 7.99 (s, 0.5H), 8.00 (s, 0.5H).

MS (ESI$^+$) m / z; 379 $[M+1]^+$

MS (ESI$^-$) m / z; 423 $[M+45]^+$ (HCOOH adduct)

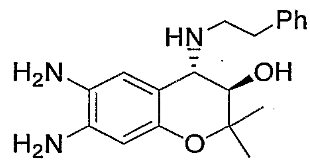
Synthesis Example 59

(*3R*,4S**)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol 1 maleate



(*3R*,4S**)-6,7-diamino-3,4-dihydro-2,2-dimethyl-4-(2-phenylethylamino)-2*H*-1-benzop

yran-3-ol



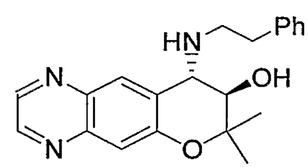
Under hydrogen stream at 1 atm, a solution of (*3R*,4S**)-6-amino-3,4-dihydro-2,2-dimethyl-7-nitro-4-(2-phenylethylamino)-2*H*-benzopyran-3-ol (10.0 g, 28.0 mmol) and 5% palladium carbon (AER type, 1 g) in ethanol (200 mL) was stirred at room temperature for 6 hours. Upon the completion of the reaction, the reaction solution was filtered through celite and concentrated to obtain the aimed product (yield: 98%).

Black amorphous product

^{1}H-NMR ($CDCl_3$) δ: 1.13 (s, 3H), 1.43 (s, 3H), 2.60-3.0 (m, 4H), 2.5-3.5 (br, 6H), 3.47 (d, *J* = 9.6 Hz, 1H), 3.51 (d, *J* = 9.6 Hz, 1H), 6.12 (s, 1H), 6.14 (s, 1H), 7.15-7.50 (m, 5H)

MS (ESI) m / z; 400[M+1]$^+$, 327 (bp).

(*3R*,4S**)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



To a solution of (*3R*,4S**)-6,7-diamino-3,4-dihydro-2,2-dimethyl-4-(2-phenylethylamino)-2*H*-benzopyran-3-ol (1.5 g, 4.58 mmol) in ethanol (30 mL), 40% aqueous glyoxal solution (997 mg, 6.87 mmol) was added, and the resulting mixture was stirred at room temperature for 30 minutes. Upon the completion of the reaction, ethyl acetate was added thereto, the resulting solution was washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated sodium chloride solution, and then dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/1) to obtain the aimed product (yield: 74%).

^{1}H-NMR ($CDCl_3$) δ: 1.26 (s, 3H), 1.56 (s, 3H), 1.60 (br s, 1H), 2.86 (t, *J* = 6.9 Hz, 1H), 2.90-3.10 (m, 3H), 3.62 (d, *J* = 10.4 Hz, 1H), 3.90 (d, *J* = 10.4 Hz, 1H), 7.24-7.40 (m, 5H), 7.42 (s, 1H), 7.94 (s, 1H), 8.05 (d, *J* = 1.7 Hz, 1H), 8.72 (d, *J* = 1.7 Hz, 1H)

MS (ESI$^+$) m / z; 350 [M+1]$^+$
MS (ESI$^-$) m / z; 349 [M-1]$^+$

(*3R*,4S**)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol 1 maleate

To a solution of (*3R*,4S**)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol (1.18 g, 3.38 mmol) in ethyl acetate (22 mL), maleic acid (471 mg, 4.06 mmol) was added at room temperature, and the resulting mixture was stirred for 10 minutes. Upon the completion of the reaction, solid product was filtered off, washed with ethyl acetate and dried to obtain the aimed product (yield: 61%).

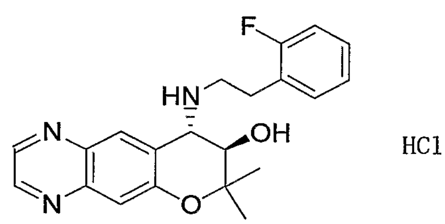
Pale gray crystals

mp: 176-179°C (decomposition)

^{1}H-NMR (DMSO-d$_6$) δ: 1.20 (s, 3H), 1.52 (s, 3H), 2.90-3.70 (m, 6H), 4.00-4.15 (m, 1H), 4.71 (d, J = 9.1 Hz, 1H), 6.07 (s, 2H), 6.34 (br s, 1H), 7.15-7.45 (m, 5H), 7.43 (s, 1H), 8.50 (s, 1H), 8.84 (s, 1H), 8.88 (s, 1H).

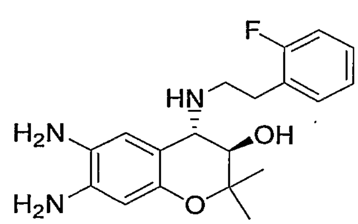
Synthesis Example 60

(*3R*,4S**)-4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol hydrochloride



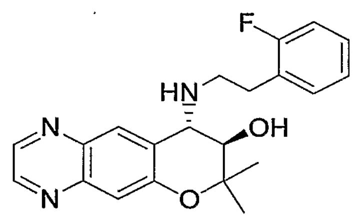
Synthesis Example 60 was carried out similarly to the process of Synthesis Example 59.

(*3R*,4S**)-6,7-diamino-4-[{2-(2-fluorophenyl)ethyl}amino]-2,2-dimethyl-3,4-dihydro-2*H*-benzopyran-3-ol



(Yield: 87%)
Black amorphous product
MS (ESI^+) m / z; 346 $[M+1]^+$
MS (ESI^-) m / z; 380 $[M+45]^+$ (HCOOH adduct)

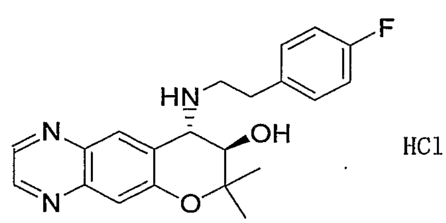
(*3R*,4S**)-4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



(Yield: 25%)
Gray amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.26 (s, 3H), 1.57 (s, 3H), 1.74 (br s, 2H), 2.85-3.15 (m, 4H), 3.61 (d, J = 10.4 Hz, 1H), 3.91 (d, J = 10.4 Hz, 1H), 7.00-7.15 (m, 3H), 7.15-7.35 (m, 2H), 7.42 (s, 1H), 7.98 (s, 1H), 8.66 (d, J = 1.7 Hz, 1H), 8.72 (d, J = 1.7 Hz, 1H).
MS (ESI^+) m / z; 368 $[M+1]^+$
MS (ESI^-) m / z; 412 $[M+45]^+$ (HCOOH adduct)

(*3R*,4S**)-4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol hydrochloride
(Yield: 95%)
Colorless crystals
mp: 265-268°C (decomposition)

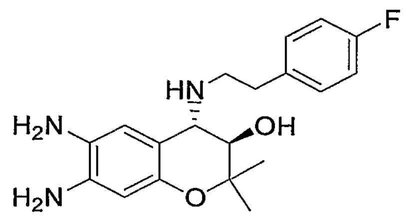
Synthesis Example 61
(*3R*,4S**)-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol hydrochloride



Synthesis Example 61 was carried out similarly to the process of Synthesis

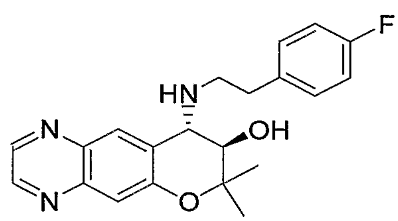
Example 59.

(*3R*,4S**)-6,7-diamino-4-[{2-(4-fluorophenyl)ethyl}amino]-2,2-dimethyl-3,4-dihydro -2*H*-1-benzopyran-3-ol



(Yield: 87%)
Black amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.13 (s, 3H), 1.45 (s, 3H), 1.90 (br s, 4H), 2.75-3.00 (m, 6H), 3.50-3.70 (m, 2H), 6.16 (s, 1H), 6.29 (s, 1H), 7.02 (t, *J* = 8.5 Hz, 2H), 7.17 (t, *J* = 8.5 Hz, 2H).

(*3R*,4S**)-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol

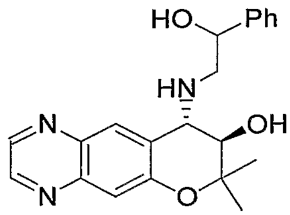


(Yield: 23%)
Pink oily product
^{1}H-NMR ($CDCl_3$) δ: 1.27 (s, 3H), 1.57 (s, 3H), 1.69 (br s, 2H), 2.83 (t, *J* = 6.9 Hz, 2H), 2.90-3.10 (m, 4H), 3.64 (d, *J* = 10.4 Hz, 1H), 3.92 (d, *J* = 10.4 Hz, 1H), 6.95-7.05 (m, 2H), 7.15-7.25 (m, 2H), 7.42 (s, 1H), 7.94 (s, 1H), 8.66 (d, *J* = 1.7 Hz, 1H), 8.73 (d, *J* = 1.7 Hz, 1H).

(*8R*,9S**)-{[2-(4-fluorophenyl)ethyl]amino}-7,7-dimethyl-8,9-dihydro-7*H*-pyrano[2,3-g]quinoxalin-8-ol hydrochloride
(Yield: 95%)
Brown crystals
mp: 191-197°C (decomposition)

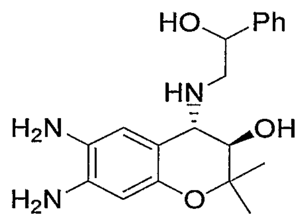
Synthesis Example 62

(*3R*,4S**)-4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



Synthesis Example 62 was carried out similarly to the process of Synthesis Example 59.

(*3R*,4S**)-6,7-diamino-4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyran-3-ol



(Yield: 92%)

Two diastereomers that can not be separated

Black amorphous product

^{1}H-NMR ($CDCl_3$) δ: 1.16 (s, 3H), 1.43 (s, 3H), 2.31 (br s, 7H), 2.70-3.05 (m, 3H), 3.50-3.70 (m, 2H), 4.70-4.80 (m, 1H), 6.16 (s, 1H), 6.53 (s, 0.5H), 6.58 (s, 0.5H), 7.20-7.40 (s, 5H).

(*3R*,4S**)-4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol

(Yield: 66%)

Two diastereomers that can not be divided

Gray amorphous product

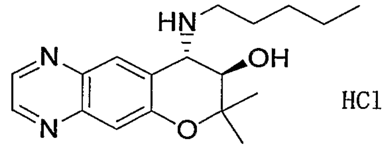
^{1}H-NMR ($CDCl_3$) δ: 1.30 (s, 3H), 1.58 (s, 1.5H), 1.59 (s, 1.5H), 1.70 (br s, 3H), 2.90-3.10 (m, 2H), 3.71 (d, J = 10.5Hz, 1H), 3.95-4.05 (m, 1H),7.20-7.45 (m, 6H), 8.10 (s, 0.5H), 8.12 (s, 0.5H), 8.64 (d, J = 1.9 Hz, 1H), 8.73 (d, J = 1.9 Hz, 1H).

MS (ESI$^+$) m / z; 366 [M+1]$^+$

MS (ESI$^-$) m / z; 410 [M+45]$^+$ (HCOOH adduct)

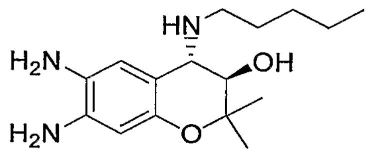
Synthesis Example 63

(*3R*,4S**)-2,2-dimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol hydrochloride



Synthesis Example 63 was carried out similarly to the process of Synthesis Example 59.

(*3R*,4S**)-6,7-diamino-2,2-dimethyl-4-pentylamino-3,4-dihydro-2*H*-1-benzopyran-3-ol

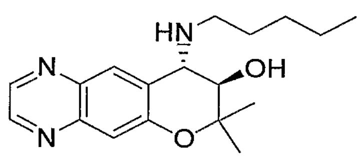


(Yield: 98%)

Brown amorphous product

^{1}H-NMR ($CDCl_3$) δ: 0.80-0.90 (m, 3H), 0.99 (s, 3H), 1.26 (s, 3H), 1.30-1.50 (m, 5H), 2.20-2.30 (m, 1H), 2.40-2.50 (m, 4H), 3.30-3.60 (m, 4H), 3.90 (br s, 2H), 4.34 (br s, 2H), 4.93 (d, J = 4.4 Hz, 1H), 5.89 (s, 1H), 6.59 (s, 1H).

(*3R*,4S**)-2,2-dimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



(Yield: 36%)

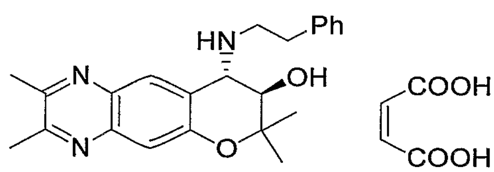
Orange amorphous product

^{1}H-NMR ($CDCl_3$) δ : 0.90 (t, *J* =7.4 Hz, 3H), 1.32 (s, 3H), 1.20-1.40 (m, 3H), 1.60-1.70 (m, 3H), 1.61 (s, 3H), 1.81 (br s, 2H), 2.60-2.90 (m, 2H), 3.68 (d, *J* = 10.2Hz, 1H), 3.93 (d, *J* = 10.2 Hz, 1H), 7.44 (s, 1H), 8.04 (s, 1H), 8.66 (d, *J* = 1.9 Hz, 1H), 8.74 (d, *J* = 1.9 Hz, 1H).

(*3R*,4S**)-2,2-dimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol

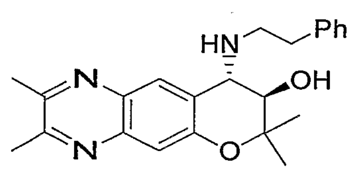
hydrochloride
(Yield: 96%)
Pale yellow crystals
mp: 209-212°C (decomposition)
MS (ESI$^+$) m / z; 316 $[M+1]^+$

Synthesis Example 64
(*3R*,4S**)-2,2,7,8-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol maleate



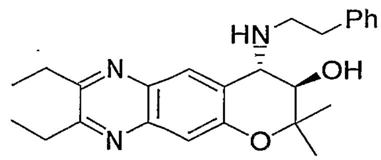
Synthesis Example 64 was carried out similarly to the process of Synthesis Example 59.

(*3R*,4S**)-2,2,7,8-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



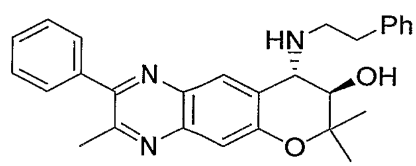
(Yield: 80%)
White amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.24 (s, 3H), 1.54 (s, 3H), 2.68 (s, 6H), 2.84 (t, J = 6.9 Hz, 2H), 2.90-3.10 (m, 4H), 3.59 (d, J = 10.2 Hz, 1H), 3.86 (d, J = 10.2 Hz, 1H), 7.20-7.40 (m, 6H), 7.82 (s, 1H).
MS (ESI$^+$) m / z; 378 $[M+1]^+$
MS (ESI$^-$) m / z; 380 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 65
(*3R*,4S**)-7,8-diethyl-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



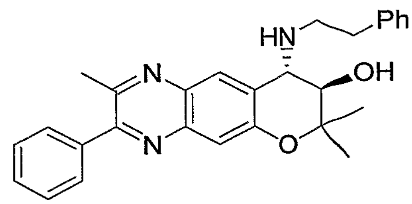
Synthesis Example 65 was carried out similarly to the process of Synthesis Example 59.
(Yield: 79%)
White solid
^{1}H-NMR ($CDCl_3$) δ: 1.23 (s, 3H), 1.39 (q, J = 6.6 Hz, 6H), 1.54 (s, 3H), 2.80-2.90 (m, 2H), 2.95-3.10 (m, 10H), 3.60 (d, J = 10.4 Hz, 1H), 3.85 (d, J = 10.4 Hz, 1H), 7.20-7.40 (m,6H), 7.81 (s, 1H).
MS (ESI$^+$) m / z; 406 $[M+1]^+$

Synthesis Example 66
(*3R*,4S**)-2,2,8-trimethyl-7-phenyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



Synthesis Example 66 was carried out similarly to the process of Synthesis Example 59.
(Yield: 33%, law polar component)
White amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.27 (s, 3H), 1.57 (s, 3H), 1.66 (br s. 2H), 2.72 (s, 3H), 2.83 (t, *J* = 6.9 Hz, 2H), 2.90-3.15 (m, 4H), 3.61 (d, *J* = 10.2 Hz, 1H), 3.88 (d, *J* = 10.2 Hz, 1H), 7.15-7.35 (m, 5H), 7.36 (s, 1H), 7.50-7.60 (m, 3H), 7.60-7.70 (m, 2H), 7.97 (s, 1H).
MS (ESI$^+$) m / z; 440 $[M+1]^+$

Synthesis Example 67
(*3R*,4S**)-2,2,7-trimethyl-8-phenyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



Synthesis Example 67 was carried out similarly to the process of Synthesis Example 59.

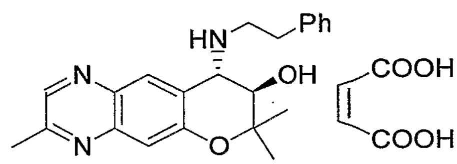
(Yield: 29%, high polar component)

^{1}H-NMR ($CDCl_3$) δ: 1.26 (s, 3H), 1.55 (s, 3H), 2.72 (s, 3H), 2.86 (t, *J* = 6.9 Hz, 2H), 2.95-3.12 (m, 4H), 3.62 (d, *J* = 10.2 Hz, 1H), 3.91 (d, *J* = 10.2 Hz, 1H), 7.20-7.35 (m, 5H), 7.42 (s, 1H), 7.45-7.55 (m, 3H), 7.60-7.70 (m, 2H), 7.90 (s, 1H).

MS (ESI$^+$) m / z; 440 $[M+1]^+$

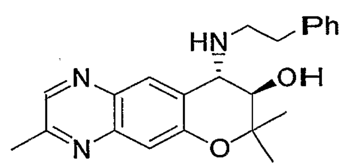
Synthesis Example 68

(*3R*,4S**)-2,2,8-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol 1 maleate



Synthesis Example 68 was carried out similarly to the process of Synthesis Example 59.

(*3R*,4S**)-2,2,8-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



(Yield: 52%)

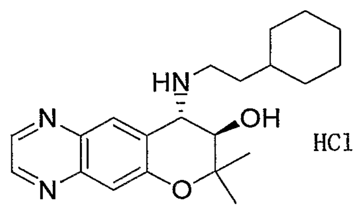
White amorphous product

^{1}H-NMR ($CDCl_3$) δ: 1.25 (s, 3H), 1.55 (s, 3H), 2.72 (s, 3H), 2.84 (t, *J* = 6.9 Hz, 2H), 2.90-3.10 (m, 4H), 3.61 (d, *J* = 10.4 Hz, 1H), 3.87 (d, *J* = 10.4 Hz, 1H), 7.15-7.40 (m, 6H), 7.89 (s, 1H), 8.54 (s, 1H).

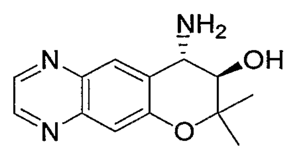
maleate

Colorless crystals
mp: 189-192°C (decomposition)

Synthesis Example 69
(*3R*,4S**)-4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol hydrochloride

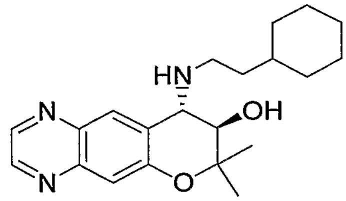


(*3R*,4S**)-4-amino-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



To a solution of (*3R*,4S**)-4,6,7-triamino-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyran-3-ol (280 mg, 1.25 mmol) in ethanol (5.6 mL), 40% aqueous glyoxal solution (226 mg, 1.56 mmol) was added, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, 1 mol/L hydrochloric acid was added thereto, the resulting solution was washed with ethyl acetate, the resulting aqueous phase was adjusted to pH 14 with 1 mol/L aqueous sodium hydroxide solution. Then, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, and dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (ethyl acetate/methanol = 10/1) to obtain the aimed product (yield: 35%).
Pale brown amorphous product
^{1}H-NMR ($CDCl_3$) δ: 1.26 (s, 3H), 1.58 (s, 3H), 2.17 (br s, 3H), 3.49 (d, J = 10.7 Hz, 1H), 3.92 (d, J = 10.7 Hz, 1H), 7.41 (s, 1H), 8.13 (s, 1H), 8.65 (s, 1H), 8.72 (s, 1H).
MS (ESI$^+$) m / z: 246 $[M+1]^+$

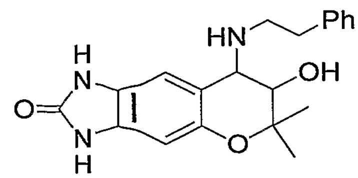
(*3R*,4S**)-4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



To a solution of (*3R*,4S**)-4-amino-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol (100 mg, 0.408 mmol) in methanol (2 mL), cyclohexylmethyl aldehyde (103 mg, 0.816 mmol) was added, and the resulting mixture was stirred at room temperature for 20 minutes. Sodium cyanoborohydride (51 mg, 0.816 mmol) was added thereto, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution; and dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 2/1) to obtain the aimed product (yield: 48%).
Yellow oily product
^{1}H-NMR ($CDCl_3$) δ: 0.80-1.00 (m, 2H), 1.10-1.40 (m, 4H), 1.31 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 1H), 1.60 (s, 3H), 1.65-1.80 (m, 6H), 2.65-2.90 (m, 2H), 3.68 (d, *J* = 10.4 Hz, 1H), 3.93 (d, *J* = 10.4 Hz, 1H), 7.44 (s, 1H), 8.04 (s, 1H), 8.67 (d, *J* = 1.9 Hz, 1H), 8.73 (d, *J* = 1.9 Hz, 1H).

(*3R*,4S**)-4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol hydrochloride
(Yield: 89%)
Yellow crystals
mp: 258-259°C (decomposition)
MS (ESI$^+$) m / z; 356 [M+1]$^+$
MS (ESI$^-$) m / z; 400[M+45]$^+$ (HCOOH adduct)

Synthesis Example 70
(±)-*trans*-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydro-pyrano[2,3-f]benzimidazol-7-one,



To a solution of (±)-*trans*-6,7-diamino-2,2-dimethyl-4-(2-phenylethylamino)-3,4-dihydro-2*H*-1-benzopyran-3-ol (500 mg, 1.53 mmol) in dioxane (7 mL), 4 mol/L hydrogen chloride/dioxane solution (0.38 mL) was added, and the resulting mixture was stirred at room temperature for 15 minutes. Then, phenyl chloroformate (0.21 mL, 1.53 mmol) and triethylamine (0.21 mL, 1.53 mmol) were added thereto, and the resulting mixture was stirred at room temperature for 1 hour. Further, triethylamine (0.63 mL, 4.58 mmol) was added thereto, and the resulting mixture was stirred at room temperature for 2 hours. Upon the completion of the reaction, 1 mol/L hydrochloric acid was added thereto and thereby adjusted to pH 7-8. Thereafter, the resulting reaction solution was extracted with ethyl acetate, washed with saturated aqueous sodium chloride solution, and then dried over sodium sulfate and concentrated. The resulting mixture was purified by silica gel column (methanol/chloroform = 1/20) to obtain the aimed product (yield: 40%).

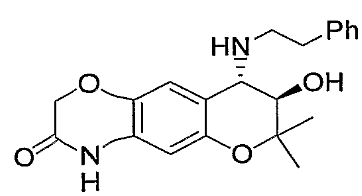
Yellow amorphous product

^{1}H-NMR ($CDCl_3$) δ: 1.15 (s, 3H), 1.30-1.41 (br, 1H), 1.45 (s, 3H), 2.71-3.96 (m, 4H), 3.51 (d, *J* = 9.9 Hz, 1H), 3.67 (d, *J* = 9.9 Hz, 1H), 6.51 (s, 1H), 7.12-7.48 (m, 7H), 7.76 (s, 1H)

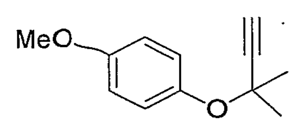
MS (ESI$^+$) m / z; 354 $[M+1]^+$

Synthesis Example 71

(*7R*,8S**)-7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-3-one

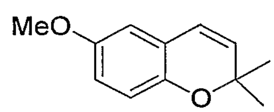


4-(1,1-dimethyl-2-propenyloxy)anisole



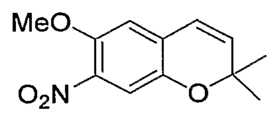
To a solution of 4-methoxyphenol (15.0 g, 121 mmol) in acetonitrile (75 mL), 1,8-diazabicyclo[5.4.0]undecene (23.9 g, 157 mmol) was added under ice cooling and the resulting mixture was stirred at 0°C for 30 minutes (Solution 1). To a solution of 2-methyl-3-buten-2-ol (11.7 g, 139 mmol) in acetonitrile (75 mL), 1,8-diazabicyclo[5.4.0]undecene (23.9 g, 157 mmol) was added under ice cooling, the resulting mixture was stirred at 0°C for 30 minutes, then trifluoroacetic anhydride (25.4 g, 121 mmol) was added and the resulting mixture was stirred at 0°C for 30 minutes (Solution 2). Copper (I) chloride (36 mg, 0.36 mmol) was added to Solution 1, and then Solution 2 was added dropwise thereto over 15 minutes. Upon the conclusion of dropwise addition, the temperature was raised to room temperature, and the mixture was stirred overnight. Upon the completion of the reaction, an aqueous ammonium chloride solution was added to the reaction solution, and the solvent was distilled off under a reduced pressure. 1 mol/L aqueous hydrochloric acid solution was added to the residue, the resulting mixture was extracted with ethyl acetate, the organic phase was washed once with 1 mol/L aqueous hydrochloric acid solution, twice with saturated aqueous sodium hydrogen carbonate solution and once with saturated sodium chloride solution. Then, the organic phase was dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was directly used for the subsequent reaction.

6-methoxy-2,2-dimethyl-2*H*-1-benzopyran



A solution of 4-(1,1-dimethyl-2-propenyloxy)anisole in 1,2-dichlorobenzene (50 mL) was stirred at 190°C for 2 hours. Upon the completion of the reaction, the solvent was distilled off under a reduced pressure. The residue was purified by column chromatography (hexane/chloroform = 3/1) and the aimed product was obtained as red oily substance (2-step, yield: 61%).
^{1}H-NMR ($CDCl_3$) δ: 1.41 (s, 6H), 3.75 (s, 3H), 5.64 (d, *J*=9.9 Hz, 1H), 6.28 (d, *J*=9.9 Hz, 1H), 6.55 (d, *J*=2.7 Hz, 1H), 6.64-6.73 (m, 2H)
LC/MS (ESI$^+$): 191[M$^+$+1]

6-methoxy-2,2-dimethyl-7-nitro-2*H*-1-benzopyran

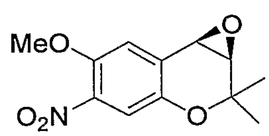


A mixed solution of acetic acid (6.2 mL) and acetic anhydride (6.2 mL) containing 6-methoxy-2,2-dimethyl-2H-1-benzopyran (3.1 g, 16.4 mmol) was cooled with ice, nitric acid (1.37 mL, 18.0 mmol) was added dropwise and then the mixture was stirred at 0°C for 1 hour. Upon the completion of the reaction, 1 mol/L aqueous sodium hydroxide solution was added to the reaction solution, the resulting solution was extracted with ethyl acetate (150 mL). The organic phase was washed twice with 1 mol/L aqueous sodium hydroxide solution and once with saturated sodium chloride solution. Then, the organic phase was dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 6/1) and the aimed product was obtained as yellow crystal (yield: 79%).

^{1}H-NMR ($CDCl_3$) δ: 1.44 (s, 6H), 3.91 (s, 3H), 5.85 (d, *J*=9.6 Hz, 1H), 6.33 (d, *J*=9.6 Hz, 1H), 6.69 (s, 1H), 7.34 (s, 1H)

LC/MS (ESI$^+$): 236 [M$^+$+1]

(*3R**, *4R**)-3,4-epoxy-6-methoxy-2,2-dimethyl-7-nitro-3,4-dihydro-2*H*-1-benzopyran

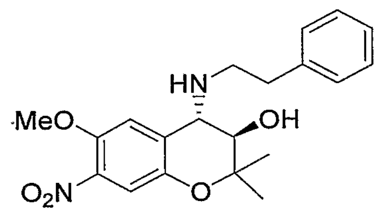


To a solution (300 mL) of acetonitrile containing 6-methoxy-2,2-dimethyl-7-nitro-2*H*-1-benzopyran (10.0 g, 42.5 mmol), *N*-methyl imidazole (0.678 mL, 8.50 mmol), Ph,Ph salen manganese complex (XX) (880 mg, 0.850 mmol) and iodosobenzene (18.7 mg, 85.0 mmol) were added at room temperature and the mixture was stirred for 2 hours. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added to the reaction solution, the resulting solution was filtered through celite. The resulting filtrate extracted with ethyl acetate. The organic phase was washed with water and sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained as yellow crystal (yield: 75%, optical purity: 99.7% ee).

^{1}H-NMR ($CDCl_3$) δ: 1.26 (s, 3H), 1.58 (s, 3H), 3.53 (d, *J*=4.3 Hz, 1H), 3.90 (d, *J*=4.3 Hz, 1H), 3.95 (s, 3H), 7.08 (s, 1H), 7.33 (s, 1H)

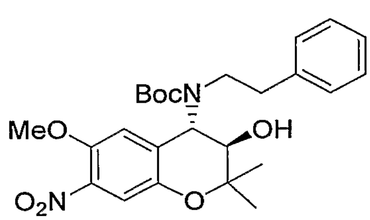
MS (EI): 251 [M^+]
HPLC: 18.6 min (enantiomer 24.1 min)
HPLC condition: chiralcel OJ-RH, MeCN/MeOH/0.01 M NaCl aq. = 1/3/5, 1.0 ml/min, 40°C, 256 nm

(*3R**,*4S**)-6-methoxy-2,2-dimethyl-7-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-3-ol



To a solution of (*3R**, *4R**)-3,4-epoxy-6-methoxy-2,2-dimethyl-7-nitro-3,4-dihydro-2*H*-1-benzopyran (2.50 g, 9.95 mmol) in 1,4-dioxane (5.0 mL), lithium perchlorate (1.06 g, 9.95 mmol) and 2-phenylethylamine (1.50 mL, 11.9 mmol) were added at room temperature and the mixture was stirred at 80 °C for 1 hour. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 6/4) and the aimed product was obtained as orange amorphous substance (quantitative yield).
^{1}H-NMR ($CDCl_3$) δ: 1.15 (s, 3H), 1.47 (s, 3H), 2.73-2.95 (m, 4H), 3.60 (d, *J*=10.0 Hz, 1H), 3.68 (d, *J*= 10.0 Hz, 1H), 3.73 (s, 3H), 6.78 (s, 1H), 7.21-7.35 (m, 6H)
MS (EI): 372[M^+]

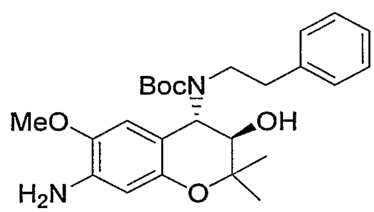
t-Butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-6-methoxy-2,2-dimethyl-7-nitro-3,4-dihydro-2*H*-1-benzopyran-4-yl carbamate



To a solution of (*3R**, *4S**)-6-methoxy-2,2-dimethyl-7-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-3-ol (407

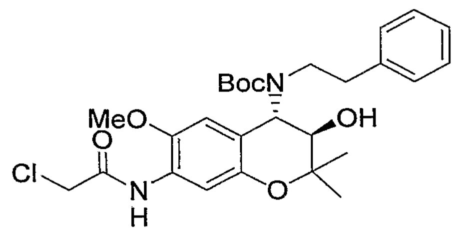
mg, 1.09 mmol) and di-*t*-butyl carbonate (477 mg, 2.19 mmol) in tetrahydrofuran (6.0 mL), triethylamine (305 mL, 2.19 mmol) was added at 0 °C and the mixture was stirred at room temperature overnight. Upon the completion of the reaction, saturated aqueous sodium carbonate solution was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with 1 mol/L hydrochloric acid aqueous solution and saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained as yellow amorphous substance (yield: 88%).
MS (EI): 473 [M^{+}+1]

t-Butyl (2-phenylethyl) (*3R**, *4S**)-7-amino-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1- benzopyran-4-yl carbamate



A solution of *t*-butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-6-methoxy-2, 2-dimethyl-7-nitro-3,4-dihydro-2*H*-1-benzopyran-4-yl carbamate (1.32 g, 2.80 mmol) and 5% palladium-carbon (132 mg) in methanol (26 mL) was stirred under hydrogen atmosphere at room temperature overnight. Upon the completion of the reaction, the reaction solution was filtered through celite. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained (yield: 94%).
Colorless solid
LC/MS (ESI^{+}): 443[M^{+}+1]

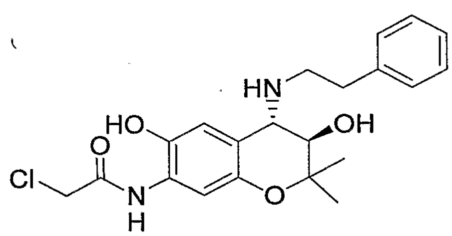
t-Butyl (2-phenylethyl) (*3R**, *4S**)-[7-(2-chloroacetylamino)-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyran-4-yl] carbamate



To a solution of *t*-butyl (2-phenylethyl) (*3R**, *4S**)-7-amino-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyran-4-yl carbamate (270 mg, 0.61 mmol) in tetrahydrofuran, triethylamine (128 μL, 0.92 mmol) and chloroacetyl chloride (73 μL, 0.92 mmol) were added at room temperature and the resulting mixture was stirred at room temperature for 2.5 hours. Upon the completion of the reaction, ethanol (1mL) and saturated aqueous ammonium chloride solution were added to the reaction solution, and the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 5/1) and the aimed product was obtained (yield: 91%).

Colorless oily product

2-Chloro-*N*-[(*3R**, *4S**)-3,6-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-7-yl]-acetamide

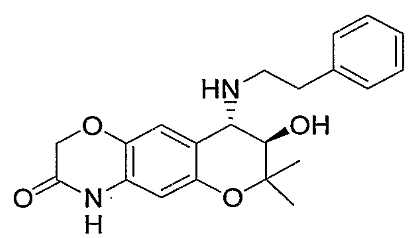


To a solution of *t*-butyl (2-phenylethyl) (*3R**, *4S**)-[7-(2-chloroacetylamino)-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyran-4-yl carbamate (251 mg, 0.48 mmol) in methylene chloride (5 mL), borane trichloride (1M solution in methylene chloride, 2.42 mL, 2.42 mmol) was added at 0 °C, and the resulting mixture was stirred for 2 hours. Upon the completion of the reaction, water was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl

acetate = 2/1) and the aimed product was obtained (yield: 70%).
Pale pink amorphous product

^{1}H-NMR ($CDCl_3$) δ: 1.33 (s, 3H), 1.44 (s, 3H), 2.75-3.00 (m, 4H), 3.50 (d, J = 9.6 Hz, 1H), 3.60 (d, J = 9.6 Hz, 1H), 4.23 (s, 2H), 6.58 (s, 1H), 6.83 (s, 1H), 7.20-7.35 (m, 5H), 8.47 (s, 1H).
MS (ESI$^+$) m / z: 405 $[M+1]^+$
MS (ESI$^-$) m / z: 403 $[M-1]^+$

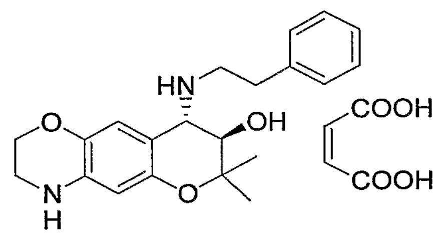
(*7R*,8S**)-7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-3-one



To a solution of 2-chloro-*N*-[(*3R**, *4S**)-3,6-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-7-yl]-acetamide (120 mg, 0.30 mmol) in methanol (1.2 mL), aqueous sodium hydroxide solution (1 mol/L, 1.5 mL) was added at room temperature, and the resulting mixture was stirred for 4 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium hydroxide solution (1 mol/L) and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/1) and the aimed product was obtained (yield: 72%).
Colorless solid
^{1}H-NMR ($CDCl_3$) δ:1.14 (s, 3H), 1.44 (s, 3H), 2.75-3.00 (m, 4H), 3.47 (d, J = 9.9 Hz, 1H), 3.56 (d, J = 9.9 Hz, 1H), 4.50 (d, J = 15.4 Hz, 1H), 4.55 (d, J = 15.4 Hz, 1H), 6.27 (s, 1H), 6.68 (s, 1H), 7.20-7.35 (m, 5H), 7.74 (s, 1H).
MS (ESI$^+$) m / z: 369 $[M+1]^+$
MS (ESI$^-$) m / z: 367 $[M-1]^+$

Synthesis Example 72

(*7R*,8S**)-6,6-dimethyl-8-[(2-phenylethyl)amino]-2,3,4,6,7,8-hexahydro-1,5-dioxa-4-aza-anthracene-7-ol maleate



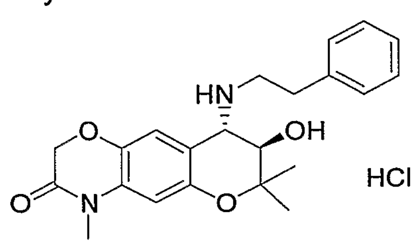
To a solution of (*7R*,8S**)-7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-3-one (42 mg, 0.11 mmol) in tetrahydrofuran (1.2 mL), lithium aluminum hydride (1M solution in tetrahydrofuran, 570 μL, 0.57 mmol) was added at room temperature, and the resulting mixture was stirred at 90°C for 1.5 hour. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. Maleic acid (13 mg, 0.11 mmol) and hexane (1mL) were added to the solution of the resulting mixture in ethyl acetate (600 μL) at room temperature, and the resulting mixture was stirred at room temperature for 15 minutes. The resulting crystal was filtered off and the aimed product was obtained (yield: 60%).

Pale brown solid

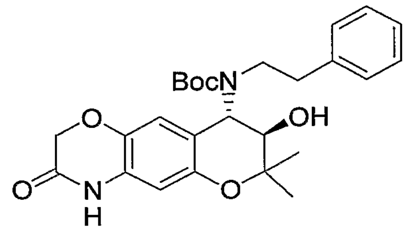
^{1}H-NMR (DMSO-d_6) δ: 1.04 (s, 3H), 1.36 (s, 3H), 2.85-3.30 (m, 6H), 3.80-3.85 (m, 1H), 4.11 (d, J = 4.2 Hz, 2H), 4.15-4.20 (m, 1H), 6.05 (s, 2H), 6.18 (s, 1H), 6.76 (s, 1H), 7.20-7.40 (m, 5H).

Synthesis Example 73

(*7R*,*8S**)-7-hydroxy-4,6,6-trimethyl-8-[(2-phanylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-3-one hydrochloride

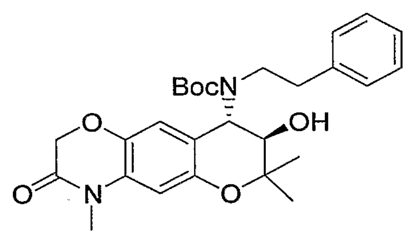


t-Butyl (2-phenylethyl) (*7R**,*8S**)-[7-hydroxy-6,6-dimethyl-3-oxo-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-8-yl] carbamate



To a solution of (*7R*,8S**)-7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-3-one (150 mg, 0.41 mmol) in tetrahydrofuran (3 mL), triethylamine (85 μL, 0.61 mmol) and di-*t*-butyl carbonate (178 mg, 0.81 mmol) were added at room temperature, and the resulting mixture was stirred at 90°C for 1.5 hour. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 3/1) and the aimed product was obtained (yield: 85%).
MS (ESI^+) m / z: 469 $[M+1]^+$
MS (ESI^-) m / z: 467 $[M-1]^+$

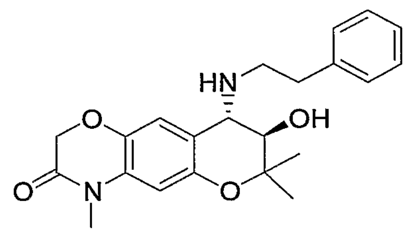
t-Butyl (2-phenylethyl) (*7R**, *8S**)-[7-hydroxy-4,6,6-trimethyl-3-oxo-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-8-yl] carbamate



To a solution of *t*-butyl (2-phenylethyl) (*7R*,8S**)-[7-hydroxy-6,6-dimethyl-3-oxo-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-8-yl] carbamate (106 mg, 0.23 mmol) in dimethylformamide (2 mL), potassium carbonate (79 mg, 0.57 mmol) and methyl iodide (28 μL, 0.46 mmol) were added at room temperature, and the resulting mixture was stirred at room temperature for 4 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with

saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 2/1) and the aimed product was obtained (yield: 100%).
MS (ESI$^+$) m / z: 505 [M+23]$^+$ (Na adduct)
MS (ESI$^-$) m / z: 527 [M+45]$^+$ (HCOOH adduct)

(*7R*,8S**)-7-hydroxy-4,6,6-trimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-3-one



To a solution of *t*-butyl (2-phenylethyl) (*7R**, *8S**)-[7-hydroxy-4,6,6-trimethyl-3-oxo-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-8-yl] carbamate (115 mg, 0.24 mmol) in ether (2.2 mL), 4 mol/L hydrogen chloride-dioxane (500 μL) was added at room temperature, and the resulting mixture was stirred at room temperature for 5 hours and then at 50°C for 30 minutes. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/2) and the aimed product was obtained (yield: 76%).
Colorless oily product
^{1}H-NMR ($CDCl_3$) δ: 1.17 (s, 3H), 1.47 (s, 3H), 2.75-3.00 (m, 4H), 3.29 (s, 3H), 3.49 (d, J = 9.9 Hz, 1H), 3.58 (d, J = 9.9 Hz, 1H), 4.52 (d, J = 15.1 Hz, 1H), 4.58 (d, J = 15.1 Hz, 1H), 6.42 (s, 1H), 6.68 (s, 1H), 7.20-7.35 (m, 5H).
MS (ESI$^+$) m / z: 383 [M+1]$^+$
MS (ESI$^-$) m / z: 427 [M+45]$^+$ (HCOOH adduct)

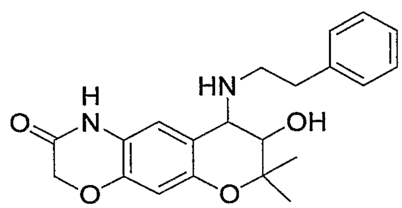
(*7R**, *8S**)-7-hydroxy-4,6,6-trimethyl-8-[(2-phanylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-3-one hydrochloride

To a solution of

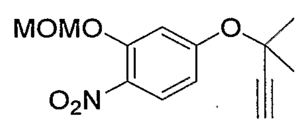
(*7R*,8S**)-7-hydroxy-4,6,6-trimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-3-one (65 mg, 0.17 mmol) in ether (2.2 mL), 4 mol/L hydrogen chloride-ethene (200 μL) was added at room temperature, and the resulting mixture was stirred at room temperature for 10 minutes. Upon the completion of the reaction, the resulting crystal was filtered off and the aimed product was obtained (yield: 93%). Pale pink solid

Synthesis Example 74

(±)-*trans*-7-Hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,6,7,8-tetrahydro-4,5-dioxa-1-aza-anthracene-2-one



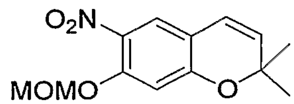
2-methoxymethoxy-4-(1,1-dimethyl-2-propionyloxy)-1-nitro-benzene



To a solution of 4-fluoro-2-nitrophenol (1.6 g, 10.2 mmol) in tetrahydrofuran (32 mL), chloromethyl methyl ether (1.23 g, 15.3 mmol) and diisopropyl ethyl amine (2.66 mL, 15.3 mmol) were added at room temperature, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. Sodium hydride (553 mg, 12.3 mmol) and 1-methyl-2-butyn-1-ol (1.23 mL, 12.7 mmol) were added to the solution of the resulting mixture in dimethylacetamide (17 mL) at 0°C, and the resulting mixture was stirred for 7 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 5/1) and the aimed product was obtained (yield: 94%).

Yellow oily product

7-Methoxymethoxy-2,2-dimethyl-6-nitro-2*H*-1-benzopyran

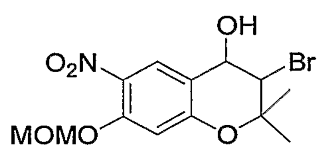


A solution of 2-methoxymethoxy-4-(1,1-dimethyl-2-propionyloxy)-1-nitro-benzene (2.1 g, 7.92 mmol) in dichlorobenzene (21 mL) was stirred at 200°C for 0.5 hour. Upon the completion of the reaction, the resulting mixture was concentrated and purified by silica gel column (hexane/ethyl acetate = 5/1). Thereby, a mixture (1:1) of the aimed product and the positional isomer was obtained (yield: 77%).

Yellow oily product

^{1}H-NMR ($CDCl_3$) δ: 1.46 (s, 6H), 3.53 (s, 1.5 H), 3.58 (s, 1.5H), 5.10 (s, 1H), 5.27 (s, 1H), 5.64 (d, J = 10.4 Hz, 0.5H), 5.74 (d, J = 10.4 Hz, 0.5H), 6.27 (d, J = 10.4 Hz, 0.5H), 6.60-6.70 (m, 1.5H), 7.67 (s, 0.5H), 7.77 (d, J = 9.1 Hz, 0.5H).

(±)-*trans*-3-Bromo-7-methoxymethoxy-2,2-dimethyl-6-nitro-3,4-dihydro-2*H*-1-benzopyran-4-ol

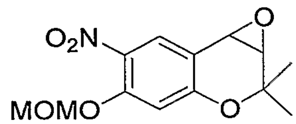


To an aqueous solution of a mixture of 7-methoxymethoxy-2,2-dimethyl-6-nitro-2*H*-1-benzopyran and the positional isomer (1.5 g, 5.65 mmol) in dimethylsulfoxide (17 mL), *N*-bromosuccinimide (1.21 g, 6.78 mmol) was added at room temperature, and the resulting mixture was stirred for 3 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 7/1) and the aimed product was obtained (yield: 27%).

Yellow solid

^{1}H-NMR ($CDCl_3$) δ: 1.45 (s, 3H), 1.63 (s, 3H), 2.73 (d, J = 4.4 Hz, 1H), 3.52 (s, 3H), 4.08 (d, J = 9.4 Hz, 1H), 4.88 (dd, J = 9.4, 4.4 Hz, 1H), 6.71 (s, 1H), 8.16 (s, 1H).

3,4-Epoxy-7-methoxymethoxy-2,2-dimethyl-6-nitro-3,4-dihydro-2*H*-1-benzopyran

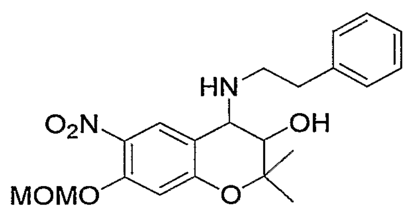


To a solution of (±)-*trans*-3-bromo-7-methoxymethoxy-2,2-dimethyl-6-nitro-3,4-dihydro-2*H*-1-benzopyran-4-ol (550 mg, 1.52 mmol) in dioxane (5.5 mL), 1 mol/L aqueous sodium hydroxide solution (1.82 mL, 1.82 mmol) was added at room temperature, and the resulting mixture was stirred for 2 hours. Upon the completion of the reaction, water was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium thiosulfate solution and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 4/1) and the aimed product was obtained (yield: 78%).

Yellow oily product

^{1}H-NMR ($CDCl_3$) δ: 1.32 (s, 3H), 1.59 (s, 3H), 3.51 (s, 3H), 3.52 (d. J = 3.9 Hz, 1H), 3.91 (d, J = 3.9 Hz, 1H), 5.26 (s, 2H), 6.73 (s, 1H), 8.05 (s, 1H).

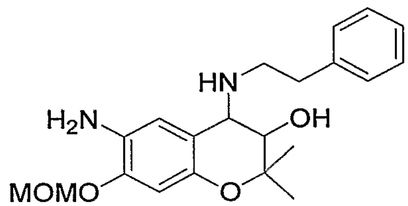
(±)-*trans*-7-Methoxymethoxy-2,2-dimethyl-6-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-3-ol



To a solution of 3,4-epoxy-7-methoxymethoxy-2,2-dimethyl-6-nitro-3,4-dihydro-2*H*-1-benzopyran (332 mg, 1.18 mmol) in dioxane (1.3 mL), lithium perchlorate (126 mg, 1.18 mmol) and 2-phenylethylamine (214 mg, 1.77 mmol) were added at room temperature, and the resulting mixture was stirred for 2 hours. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 3/1) and the aimed product was obtained (yield: 73%).

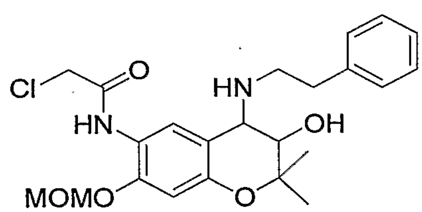
Yellow oily product
^{1}H-NMR ($CDCl_3$) δ: 1.19 (s, 3H), 1.47 (s, 3H), 2.75-3.00 (m, 4H), 3.45-3.55 (m, 2H), 3.50 (s, 3H), 5.24 (s, 2H), 6.66 (s, 1H), 7.15-7.40 (m, 5H), 7.72 (s, 1H)

(±)-*trans*-6-amino-7-Methoxymethoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-3-ol



To a solution of (±)-*trans*-7-methoxymethoxy-2,2-dimethyl-6-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran (265 mg, 0.66 mmol) in ethanol (5 mL), 5% palladium-carbon (AER type, 13 mg) was added at room temperature, and the resulting mixture was stirred under hydrogen stream overnight. Upon the completion of the reaction, the resulting solution was filtered through celite, concentrated, and the aimed product was obtained (yield: 98%).
Brown oily product
^{1}H-NMR ($CDCl_3$) δ: 1.13 (s, 3H), 1.43 (s, 3H), 2.70-3.05 (m, 8H), 3.51 (s, 3H), 3.52-3.60 (m, 2H), 5.12 (s, 2H), 6.21 (s, 1H), 6.51 (s, 1H), 7.20-7.50 (m, 5H).

2-Chloro-*N*-[(±)-*trans*-3-hydroxy-7-methoxymethoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-6-yl]-acetamide



To *trans*-6-amino-7-Methoxymethoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-3-ol (242 mg, 0.65 mmol) in ethyl acetate-dimethylformamide mixed solution (5 mL), 4 M hydrogen chloride-dioxane solution (194 μL, 0.78 mmol) was added at 0°C, and the resulting mixture was stirred for 5 minutes. Chloroacetyl chloride (88 mg, 0.78 mmol) was added thereto, and the resulting mixture was stirred

for 15 minutes. Upon the completion of the reaction, ethanol and saturated aqueous sodium hydrogencarbonate solution were added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/1) and the aimed product was obtained (yield: 79%).

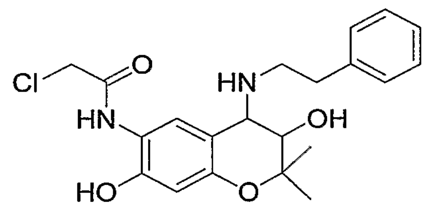
Pale pink oily product

^{1}H-NMR ($CDCl_3$) δ: 1.17 (s, 3H), 1.45 (s, 3H), 2.75-3.00 (m, 4H), 3.43 (d, J = 9.9 Hz, 1H), 3.50 (s, 3H), 3.59 (d, J = 9.9 Hz, 1H), 4.20 (s, 2H), 5.19 (s, 2H), 6.61 (s, 1H), 7.15-7.30 (m, 5H), 8.14 (s, 1H), 8.73 (s, 1H).

MS (ESI^+) m / z: 449 $[M+1]^+$

MS (ESI^-) m / z: 447 $[M-1]^+$

2-Chloro-*N*-[(±)-*trans*-3,7-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-6-yl]-acetamide



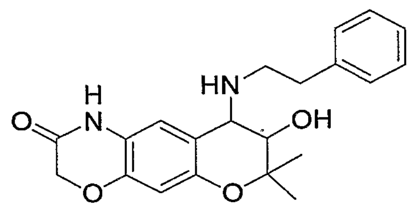
To a solution of 2-Chloro-*N*-[(±)-*trans*-3-hydroxy-7-methoxymethoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-6-yl]-acetamide (228 mg, 0.51 mmol) in methylene chloride (6 mL), boron tribromide (1 M solution in methylene chloride, 2.42 mL, 2.42 mmol) was added at 0°C, and the resulting mixture was stirred for 2 hours. Upon the completion of the reaction, methanol and saturated aqueous sodium hydrogencarbonate solution were added thereto, and the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated aqueous sodium chloride solution, dried over magnesium sulfate and concentrated to obtain the aimed product (yield: 100%).

Colorless amorphous product

MS (ESI^+) m / z: 405 $[M+1]^+$

MS (ESI^-) m / z: 403 $[M-1]^+$

(±)-*trans*-7-Hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,6,7,8-tetrahydro-4,5-dioxa-1-aza-anthracene-2-one



To a solution of 2-Chloro-*N*-[(±)-*trans*-3,7-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-6-yl]-acetamide (187 mg, 0.46 mmol) in methanol (2 mL), aqueous sodium hydroxide solution (1 mol/L, 1.8 mL) was added at room temperature, and the resulting mixture was stirred for 3 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with 1 mol/L aqueous sodium hydroxide solution and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/3) and the aimed product was obtained (yield: 61%).

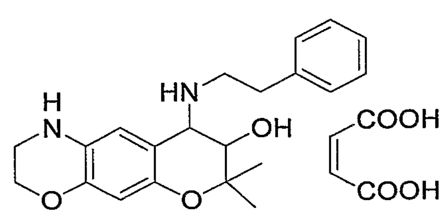
Colorless oily product

^{1}H-NMR ($CDCl_3$) δ: 1.14 (s, 3H), 1.45 (s, 3H), 2.65-3.00 (m, 4H), 3.53 (d. J = 9.9 Hz, 1H), 3.57 (d, J = 9.9 Hz, 1H), 4.50 (d, J = 15.4 Hz, 1H), 4.56 (d, J = 15.4 Hz, 1H), 5.99 (s, 1H), 6.40 (s, 1H), 7.15-7.40 (m, 5H).

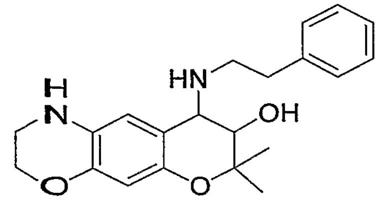
MS (ESI$^+$) m / z: 369 [M+1]$^+$

Synthesis Example 75

(±)-*trans*-6,6-Dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-aza-anthracene-7-ol maleate



(±)-*trans*-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-aza-anthracene-7-ol



To (±)-*trans*-7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,6,7,8-tetrahydro-4,5-dioxa-1-aza-anthracene-2-one (67 mg, 0.18 mmol), lithium aluminum hydride (1M solution in tetrahydrofuran, 910 μL, 0.91 mmol) was added at room temperature, and the resulting mixture was stirred at 90°C for 0.5 hour. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (ethyl acetate) and the aimed product was obtained (yield: 59%).

Colorless oily product

^{1}H-NMR ($CDCl_3$) δ: 1.13 (s, 3H), 1.43 (s, 3H), 2.75-3.00 (m, 4H), 3.30-3.35 (m, 2H), 3.50-3.70 (m, 2H), 4.15-4.25 (m, 2H), 6.12 (s, 1H). 6.25 (s, 1H), 7.20-7.35 (m, 5H).

MS (ESI$^+$) m / z: 355 $[M+1]^+$

MS (ESI$^-$) m / z: 389 $[M+45]^+$ (HCOOH adduct)

(±)-*trans*-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-aza-anthracene-7-ol maleate

To a solution of (±)-*trans*-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-aza-anthracene-7-ol in ethyl acetate (800 μL), maleic acid (14 mg, 0.12 mmol) was added at room temperature, and the resulting mixture was stirred for 10 minutes. Hexane (1 mL) was added thereto, and the resulting mixture was stirred at 0°C for 30 minutes. The resulting crystal was filtered off and the aimed product was obtained (yield: 73%).

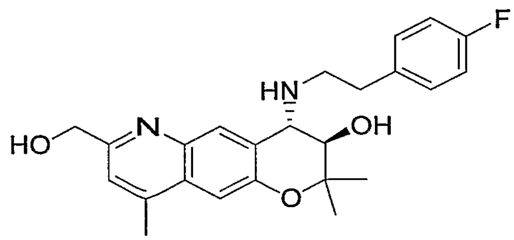
Pale gray crystals

mp;162-162°C (decomposition)

^{1}H-NMR (DMSO-d_6) δ : 1.04 (s, 3H), 1.36 (s, 3H), 2.85-3.30 (m, 6H), 3.80-3.85 (m, 1H), 4.11 (d, J = 4.2 Hz, 2H), 4.15-4.20 (m, 1H), 6.05 (s, 2H), 6.18 (s, 1H), 6.76 (s, 1H), 7.20-7.40 (m, 5H).

Synthesis Example 76

(*3R*,4S**)-4-{[2-(4-fluorophenyl)ethyl]amino}-7-hydroxymethyl-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



This compound was synthesized according to the process of Synthesis Example 18. (Yield: 42%)

White crystals

mp;147-152°C

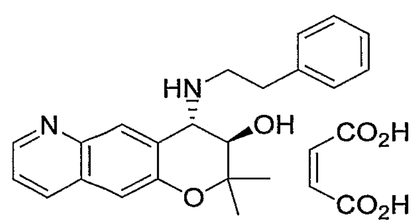
^{1}H-NMR($CDCl_3$); 1.26(s, 3H), 1.56(s, 3H), 2.59(s, 3H), 2.84-2.86(m, 2H), 2.92-3.09(m, 2H), 3.64(d, *J* = 10.5 Hz, 1H), 3.89(d, *J* = 10.2 Hz, 1H), 4.83(s, 2H), 6.99-7.05(m, 3H), 7.12-7.23(m, 2H), 7.29(s, 1H), 7.81(s, 1H)

MS(ESI^{+})m/z; 411 $[M+1]^{+}$

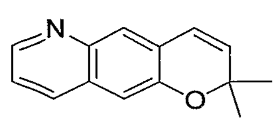
MS(ESI^{-})m/z; 455 $[M+45]^{+}$ (HCOOH adduct)

Synthesis Example 77

(*3R*,4S**)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



2,2-dimethyl-2*H*-pyrano[2,3-g]quinoline



Under nitrogen atmosphere, to a solution of 6-amino-2,2-dimethylchromene (3.88 g, 22.1 mmol) and ruthenium trichloride (55.0 mg, 0.265 mmol) in dimethylene glycol dimethyl ether (8 mL), 1,3-propanediol (0.639 mL, 8.84 mmol) and tri-*n*-butyl

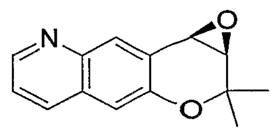
phosphine (0.132 mL, 0.530 mmol) were added at room temperature, and the resulting mixture was stirred at 180°C for 5 hours. Upon the completion of the reaction, ruthenium complex was removed by florisil column, and solvent was distilled off. The residue was purified by medium pressure column chromatography (hexane/ethyl acetate =5/1) and the aimed product was obtained (yield: 59%).

Gray amorphous product

^{1}H-NMR($CDCl_3$); 1.49(s, 6H), 5.91(d, *J* = 9.9 Hz, 1H), 6.59(d, *J* = 9.9 Hz, 1H), 7.08(s, 1H), 7.24-7.28(m, 1H), 7.67(s, 1H), 7.93(d, *J* = 8.0 Hz, 1H), 8.70(dd, *J* = 4.1 Hz, 1.7Hz, 1H)

MS(ESI$^+$)m/z; 212 $[M+1]^+$

(*3R*,4R**)-3,4-epoxy-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline



This compound was synthesized according to the process of Synthesis Example 12.

(Yield: 65%)

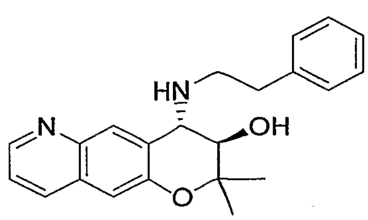
CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 7.3 min.

Brown solid

^{1}H-NMR($CDCl_3$); 1.30(s, 3H), 1.65(s, 3H), 3.61(d, *J* = 4.4 Hz, 1H), 4.18(d, *J* = 4.4 Hz, 1H), 7.17(s, 1H), 7.34 (dd, *J* = 8.5 Hz, 4.4 Hz, 1H),8.01(d, *J* = 7.7 Hz, 1H), 8.12(s, 1H), 8.79(dd, *J* = 4.1 Hz, 1.7Hz, 1H)

MS(ESI$^+$)m/z; 228 $[M+1]^+$

(*3R*,4S**)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



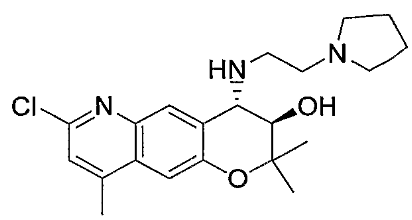
(Yield: 58%)

MS(ESI$^+$)m/z; 349 $[M+1]^+$

MS(ESI$^-$)m/z; 393 [M+45]$^+$ (HCOOH adduct)

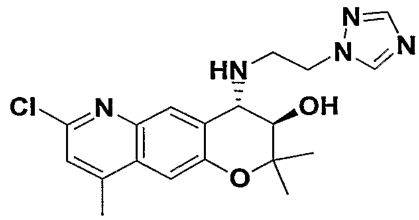
(*3R*,4S**)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate
(Yield: 79%)
White crystals
mp;187-192°C (decomposition)
^{1}H-NMR(DMSO-d$_6$); 1.16(s, 3H), 1.50(s, 3H), 2.94-3.00(m, 1H), 3.09-3.20(m, 2H), 3.34-3.37(m, 1H), 4.07-4.11(m, 1H), 4.69(d, *J* = 9.4 Hz, 1H), 6.05(s, 2H), 6.32(br s, 1H), 7.23-7.39(m, 6H), 7.49(dd, *J* = 8.3Hz, 4.1 Hz, 1H), 8.22(d, *J* = 8.3 Hz, 1H), 8.44(s, 1H), 8.80(d, *J* = 3.9 Hz, 1H)

Synthesis Example 78
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[2-(1-pyrrolidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



This compound was synthesized according to the process of Synthesis Example 19.
(Yield: 30%)
Orange amorphous product
^{1}H-NMR (CDCl$_3$) δ: 1.19 (s, 3H), 1.50 (s, 3H), 2.05-2.15 (br, 2H), 2.49 (s, 3H), 3.09-3.32 (m, 10H), 4.60-5.20 (br, 2H), 7.06 (s, 1H), 7.11 (s, 1H), 7.88 (s, 1H)
MS (EI$^+$) m / z ; 390[M+1]$^+$

Synthesis Example 79
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-{[2-(1,2,4-triazol-1-yl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



This compound was synthesized according to the process of Synthesis Example 19.

(Yield: 32%)

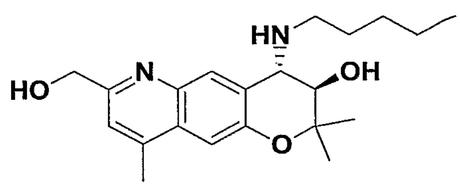
Pale yellow solid

^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 3H), 1.57 (s, 3H), 2.00 (br), 2.58 (s, 3H), 3.23-3.35 (m, 2H), 3.63 (d, *J* = 10.2 Hz, 1H), 3.90 (d, *J* = 10.2 Hz, 1H), 4.29-4.38 (m, 2H), 7.15 (s, 1H), 7.27 (s, 1H), 7.99 (m, 2H), 8.18 (s, 1H)

MS (ESI$^+$) m / z; 388 $[M+1]^+$

Synthesis Example 80

(*3R*,4S**)-7-hydroxymethyl-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



This compound was synthesized according to the process of Synthesis Example 18.

(Yield: 38%)

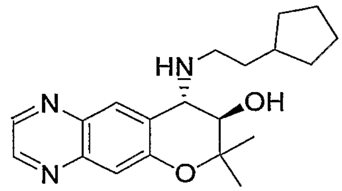
Pale yellow crystals

^{1}H-NMR ($CDCl_3$) δ: 0.88-0.93 (m, 3H), 1.29 (s, 3H), 1.33-1.37 (m, 4H), 1.59 (s, 3H), 1.60 (m, 2H), 2.60 (s, 3H), 2.66-2.84 (m, 2H), 3.68 (d, *J* = 10.5 Hz, 1H), 3.94 (d, *J* = 10.5 Hz, 1H), 4.83 (s, 2H), 7.04 (s, 1H), 7.31 (s, 1H), 7.99 (s, 1H)

MS (ESI$^+$) m / z; 359$[M+1]^+$

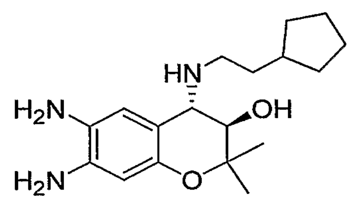
Synthesis Example 81

(*3R*,4S**)-4-[(2-cyclopentylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol



This compound was synthesized according to the process of Synthesis Example 59.

(*3R*,4S**)-6,7-diamino-4-[(2-cyclopentylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyran-3-ol



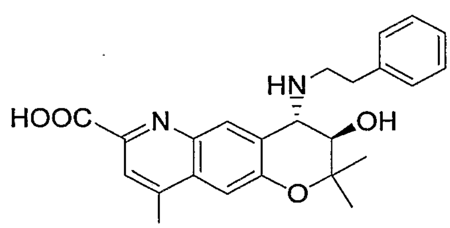
Black amorphous product

(*3R*,4S**)-4-[(2-cyclopentylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol

^{1}H-NMR ($CDCl_3$) δ: 1.05(m, 2H), 1.31(s, 3H), 1.50-1.90(m, 9H), 1.59(s, 3H), 2.60-2.90(m, 2H), 3.37(brs, 1H), 3.68(d, J = 10.4 Hz, 1H), 3.93 (d, J = 10.4 Hz, 1H), 7.44 (s, 1H), 8.03 (s, 1H), 8.66 (d, J = 1.7 Hz, 1H), 8.74 (d, J = 1.7 Hz, 1H).

Synthesis Example 82

(*3R*,4S**)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carboxylic acid



To a solution of (*3R*,4S**)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile described in Synthesis Example 14 (465 mg, 1.20 mmol) in ethanol (5 mL), aqueous sodium hydroxide solution (3 mol/L, 5 mL) was added at room temperature, and the resulting mixture was stirred for 2 hours with reflux under

heating. After cooling to room temperature, the resulting solution was neutralized with 1 mol/L hydrochloric acid, precipitated brown solid was filtered off and the aimed product was obtained (yield: 90%).

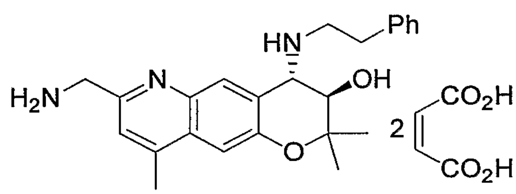
Brown solid

^{1}H-NMR ($CDCl_3$) δ: 1.07 (s, 3H), 1.41 (s, 3H), 2.46 (s, 3H), 2.89-3.08 (br, 2H), 3.10-3.28 (br, 2H), 4.03-4.22 (br, 1H), 4.30-4.44 (br, 1H), 7.01-7.54 (m, 7H), 7.86 (s, 1H), 8.51-8.73(br, 1H)

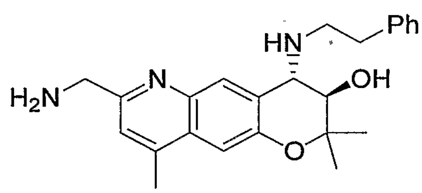
MS (EI$^+$) m / z; 407 [M+1]$^+$

Synthesis Example 83

(*3R*,4S**)-7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 2 maleate



(*3R*,4S**)-7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



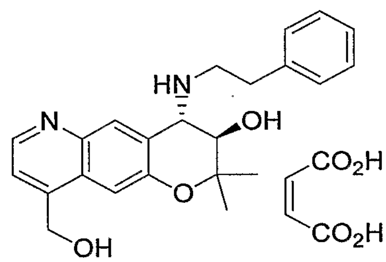
To a solution of (*3R*,4S**)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile described in Synthesis Example 14 (110 mg, 0.283 mmol) in acetic acid (5 mL), 10% Pd/C (22 mg) was added at room temperature, and the resulting mixture was stirred for 2 hours under hydrogen atmosphere. Upon the completion of the reaction, the resulting solution was filtered through celite, the solvent was distilled off and then aqueous sodium carbonate solution was added to the residue, and the resulting solution was extracted with chloroform, dried over anhydrous magnesium sulfate, and the solvent was distilled off to obtain crude product of (*3R*,4S**)-7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol (75.1 mg).

^{1}H-NMR($CDCl_3$) δ; 1.14(s, 3H), 1.46(s, 3H), 2.48(s, 3H), 2.73(t, *J* = 6.6 Hz, 2H),

2.88-2.95(m, 2H), 3.53(d, J = 10.5 Hz, 1H), 3.77(d, J = 10.2 Hz, 1H), 3.98(s, 2H), 7.04(s, 1H), 7.12-7.23(m, 6H), 7.84(s, 1H)
MS(ESI$^+$)m/z; 392 [M+1]$^+$

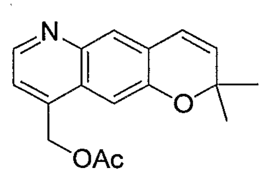
(*3R*,4S**)-7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 2 maleate
(2-steps yield: 14%)
Brown crystals
mp;136-140°C
^{1}H-NMR(DMSO-d$_6$) δ; 1.18(s, 3H), 1.49(s, 3H), 2.60(s, 3H), 2.90-3.00(m, 2H), 3.24-3.35(m, 2H), 4.02(brs, 1H), 4.33(s, 2H), 4.51(brs, 1H), 6.04(s, 4H), 7.21-7.42(m, 7H), 8.32(brs, 2H), 8.36(s, 1H)

Synthesis Example 84
(*3R*,4S**)-9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate



This compound was synthesized according to the process of Synthesis Example 18.

(2,2-Dimethyl-2*H*-pyrano[2,3-g]quinolin-9-yl)-methylacetate



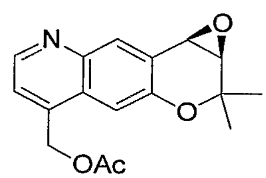
To a solution of 2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline described in Synthesis Example 1 (3.30 mg, 14.6 mmol) in chloroform (33 mL), a solution of *m*-chloroperbenzoic acid (5.54 g, 19.5 mmol) in chloroform (13.2 mL)-methanol (3.3 mL) was added dropwise at room temperature, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, aqueous

sodium thiosulfate solution was added thereto and the resulting solution was extracted therewith. The resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, acetic anhydride (46 mL) was added to the residue at room temperature, and the resulting mixture was stirred at 150°C for 1 hour. Upon the completion of the reaction, acetic anhydride was distilled off, the residue was neutralized with aqueous sodium carbonate solution, extracted with chloroform, and the resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 1/1) and the aimed product was obtained (yield: 34%).

^{1}H-NMR($CDCl_3$) δ; 1.41(s, 6H), 2.09(s, 3H), 5.37(s, 2H), 5.84(d, *J* = 9.9 Hz, 1H), 6.49(d, *J* = 9.9 Hz, 1H), 7.09(s, 1H), 7.24(d, *J* = 4.4 Hz, 1H), 7.66(s, 1H), 8.61(d, *J* = 4.4 Hz, 1H)

MS(ESI$^+$)m/z; 284 $[M+1]^+$

(*3R*,4R**)-(3,4-epoxy-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-9-yl)-methylacetate



(Yield: 58%)

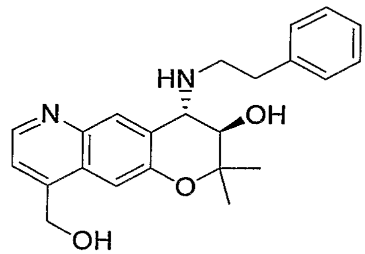
99.5% ee; CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 9.5 min.

Pale yellow solid

^{1}H-NMR($CDCl_3$) δ 1.31(s, 3H), 1.66(s, 3H), 2.18(s, 3H), 3.62(d, *J* = 4.4 Hz, 1H), 4.18(d, *J* = 4.4 Hz, 1H), 5.47(d, *J* = 2.2 Hz, 2H), 7.28(s, 1H), 7.38(d, *J* = 4.1 Hz, 1H), 8.16(s, 1H), 8.78(d, *J* = 4.4 Hz, 1H)

MS(ESI$^+$)m/z; 300 $[M+1]^+$

(*3R*,4S**)-9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol



(Yield: 80%)

Brown amorphous product

^{1}H-NMR($CDCl_3$) δ; 1.23(s, 3H), 1.52(s, 3H), 2.77-2.81(m, 2H), 2.90-3.04(m, 2H), 3.58(d, *J* = 10.5 Hz, 1H), 3.83(d, *J* = 10.4 Hz, 1H), 5.08(s, 2H), 7.17-7.21(m, 4H), 7.26-7.31(m, 2H), 7.44(d, *J* = 4.4 Hz, 1H), 7.98(s, 1H), 8.65(t, *J* = 4.7 Hz, 1H)

MS(ESI$^+$)m/z; 379 $[M+1]^+$

MS(ESI$^-$)m/z; 423 $[M+45]^+$ (HCOOH adduct)

(*3R*,4S**)-9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate

(Yield: 88%)

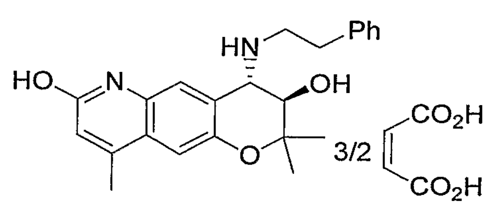
White crystals

mp;163-169°C (decomposition)

^{1}H-NMR(DMSO-d_6) δ; 1.17(s, 3H), 1.50(s, 3H), 2.94-3.01(m, 1H), 3.09-3.21(m, 2H), 3.35-3.38(m, 2H), 4.09(dd, *J* = 9.6 Hz, 6.3 Hz, 1H), 4.72(d, *J* = 9.4 Hz, 1H), 4.91(s, 2H), 5.57(brs, 1H), 6.08(s, 2H), 6.34(d, *J* = 5.5 Hz, 1H), 7.23-7.39(m, 6H), 7.52(d, *J* = 4.4 Hz, 1H), 8.45(s, 1H), 8.77(d, *J* = 4.4 Hz, 1H)

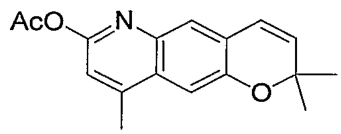
Synthesis Example 85

(*3R*,4S**)-2,2,9-trimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3,7-diol 3/2 maleate



This compound was synthesized according to the process of Synthesis Example 18.

(2,2,9-Trimethyl-2*H*-pyrano[2,3-g]quinolin-7-yl)-acetate



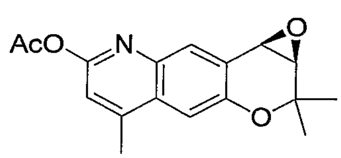
To a solution of 2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline described in Synthesis Example 1 (3.30 g, 14.6 mmol) in chloroform (33 mL), a solution of *m*-chloroperbenzoic acid (5.54 g, 19.5 mmol) in chloroform (13.2 mL)-methanol (3.3 mL) was added dropwise at room temperature, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added thereto and the resulting solution was extracted therewith. The resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, acetic anhydride (46 mL) was added to the residue at room temperature, and the resulting mixture was stirred at 150°C for 1 hour. Upon the completion of the reaction, acetic anhydride was distilled off, the residue was neutralized with aqueous sodium carbonate solution, extracted with chloroform, and the resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 1/1) and the aimed product was obtained (yield: 23%).

Red oily product

^{1}H-NMR($CDCl_3$) δ; 1.49(s, 6H), 2.395(s, 3H), 2.404(s, 3H), 5.90(d, J = 9.9 Hz, 1H), 6.58(d, J = 9.9 Hz, 1H), 7.23(s, 1H), 7.74(s, 1H), 8.48(s, 1H)

MS(ESI$^+$)m/z; 284 [M+1]$^+$

[(3*R**,4*R**)-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-7-yl]-acetate



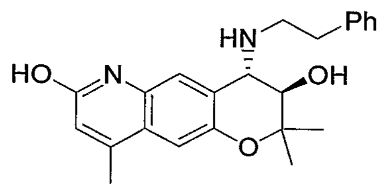
(Yield: 37%)

CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 6.6 min.

Brown amorphous product

^{1}H-NMR($CDCl_3$) δ ; 1.29(s, 3H), 1.64(s, 3H), 2.41(s, 6H), 3.60(d, J = 4.4 Hz, 1H), 4.15(d, J = 4.1 Hz, 1H), 7.31(s, 1H), 8.10(s, 1H), 8.47(s, 1H)
MS(ESI$^+$)m/z; 300 [M+1]$^+$

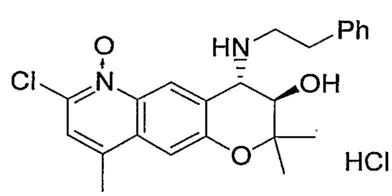
(*3R*,4S**)-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3,7-diol



(Yield: 46%)
Brown amorphous product
^{1}H-NMR($CDCl_3$) δ; 1.25(s, 3H), 2.05(s, 3H), 2.48(s, 3H), 2.80(t, J = 6.6 Hz, 2H), 2.93-3.12(m, 2H), 3.58(d, J = 10.2 Hz, 1H), 3.84(d, J = 10.2 Hz, 1H), 7.12-7.25(m, 6H), 8.02(s, 1H), 8.66(s, 1H)
MS(ESI$^+$)m/z; 379 [M+1]$^+$
MS(ESI$^-$)m/z; 377 [M-1]$^+$

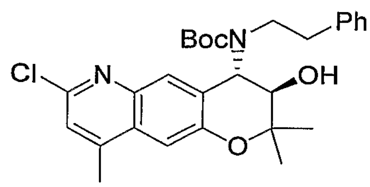
(*3R*,4S**)-2,2,9-trimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3,7-diol 3/2 maleate
(Yield: 70%)
White crystals
mp;184-188°C (decomposition)
^{1}H-NMR(DMSO-d_6) δ; 1.16(s, 3H), 1.49(s, 3H), 2.35(s, 3H), 2.94-3.00(m, 1H), 3.10-3.22(m, 2H), 3.36-3.42(m, 1H), 4.04-4.10 (m, 1H), 4.66(d, J = 9.4 Hz, 1H), 6.12(s, 3H), 6.33(d, J = 5.8 Hz, 1H), 7.23-7.36(m, 6H), 8.30(s, 1H), 8.49(s, 1H), 10.12(s, 1H)

Synthesis Example 86
(*3R*,4S**)-7-chloro-2,2,9-trimethyl-6λ5-oxy-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride



t-Butyl (2-phenylethyl)

[(*3R*,4S**)-7-chloro-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-yl] carbamate

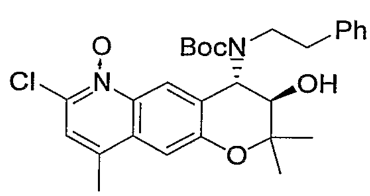


To a solution of (*3R*,4S**)-7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-3-ol described in Synthesis Example 19 (391 mg, 0.99 mmol) and di-*t*-butyl dicarbonate (430 mg, 1.97 mmol) in tetrahydrofuran (8 mL), triethylethylamine (600 μL, 4.29 mmol) was added dropwise, and the resulting mixture was stirred at room temperature for 2 hours. Further, di-*t*-butyl dicarbonate (430 mg, 1.97 mmol) was added thereto at room temperature, and the resulting mixture was stirred overnight. Upon the completion of the reaction, aqueous sodium carbonate solution was added thereto and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 10/1) and the aimed product was obtained (yield: 87%).

MS(ESI^+)m/z; 497 $[M+1]^+$

MS(ESI^-)m/z; 541 $[M+45]^+$ (HCOOH adduct)

t-butyl (2-phenylethyl)
[(*3R*,4S**)-7-chloro-3-hydroxy-2,2,9-trimethyl-6λ5-oxy-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-yl] carbamate



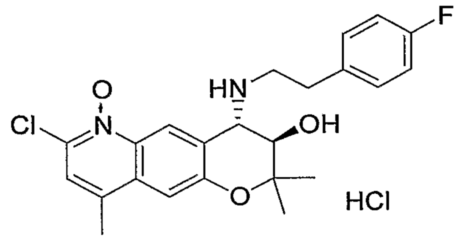
To a solution of *t*-butyl (2-phenylethyl) [(*3R*,4S**)-7-chloro-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-yl] carbamate (100 mg, 0.20 mmol) in chlroform (1 mL), a solution of *m*-chloroperbenzoic acid (75.9 mg, 0.44 mmol) in chloroform (0.4 mL)-methanol (0.1 mL) was added dropwise at room temperature, and the resulting mixture was stirred at room temperature for 30 minutes. At room temperature, a solution of

m-chloroperbenzoic acid (75.9 mg, 0.44 mmol) in chloroform (0.4 mL) was further added thereto and the resulting mixture was stirred overnight. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added thereto and the resulting solution was extracted therewith. The resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 3/1 to 1/1) and the aimed product was obtained (yield: 41%).
MS(ESI^+)m/z; 513 $[M+1]^+$
MS(ESI^-)m/z; 557 $[M+45]^+$ (HCOOH adduct)

(*3R*,4S**)-7-chloro-2,2,9-trimethyl-6λ5-oxy-4-[(2-phenylethyl)amino)]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride

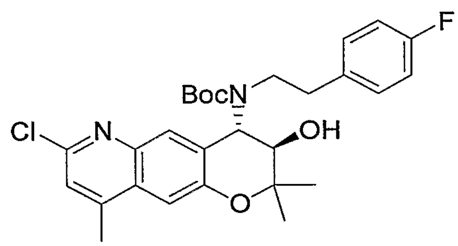
To a solution of *t*-butyl (2-phenylethyl) [(*3R*,4S**)-7-chloro-3-hydroxy-2,2,9-trimethyl-6λ5-oxy-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-yl] carbamate (41.7 mg, 0.081 mmol) in 1,4-dioxane (0.2 mL), 4 mol/L hydrogen chloride-dioxane solution (0.42 mL) was added at room temperature, and the resulting mixture was stirred at 80°C for 1 hour. Upon the completion of the reaction, precipitated solid was filtered off and washed with di-isopropyl ether to obtain the aimed product (yield: 72%).
White crystals
mp;174-179°C (decomposition)
^{1}H-NMR(DMSO-d_6) δ; 1.14(s, 3H), 1.49(s, 3H), 2.53(s, 3H), 3.00-3.55(m, 4H), 4.21(d, J = 9.1 Hz, 1H), 4.76(brs, 1H), 7.23-7.31(m, 6H), 7.45(s, 1H), 7.65(s, 1H), 9.08(s, 1H), 9.37(brs, 1H), 10.16(brs, 1H)
MS(ESI^+)m/z; 413, 415 $[M+1]^+$
MS(ESI^-)m/z; 457, 459 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 87
(*3R*,4S**)-7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-6λ5-oxy-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride



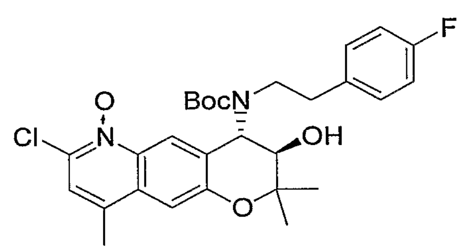
This compound was synthesized by using the compound of Synthesis Example 23 similarly to the process of Synthesis Example 86.

t-butyl [2-(4-fluorophenyl)ethyl] [(*3R*,4S**)-7-chloro-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-yl] carbamate



MS(ESI$^+$)m/z; 515, 517 [M+1]$^+$
MS(ESI$^-$)m/z; 559, 561 [M+45]$^+$ (HCOOH adduct)

t-butyl [2-(4-fluorophenyl)ethyl] [(*3R*,4S**)-7-chloro-3-hydroxy-2,2,9-trimethyl-6λ5-oxy-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-yl] carbamate



(2-steps yield: 30%).
MS(ESI$^+$)m/z; 531, 533 [M+1]$^+$
MS(ESI$^-$)m/z; 575, 577 [M+45]$^+$ (HCOOH adduct)

(*3R*,4S**)-7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-6λ5-oxy-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride

(yield: 71%).

Pale yellow crystals

mp;193-198°C (decomposition)

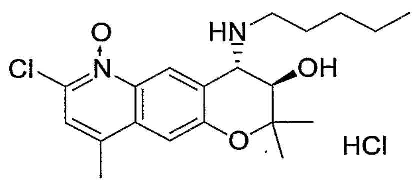
^{1}H-NMR(DMSO-d_6) δ; 1.14(s, 3H), 1.49(s, 3H), 2.53(s, 3H), 2.96-3.06(m, 1H), 3.16-3.18(m, 2H), 3.36(brs, 1H), 4.19-4.22(m, 1H), 4.75-4.78(m, 1H), 7.13(t, *J* = 9.08 Hz, 2H), 7.26-7.31(m, 2H), 7.45(s, 1H), 7.65(s, 1H), 9.06(s, 1H), 9.37(brs, 1H), 10.16(brs, 1H)

MS(ESI$^+$)m/z; 431, 433 [M+1]$^+$

MS(ESI$^-$)m/z; 475, 477 [M+45]$^+$

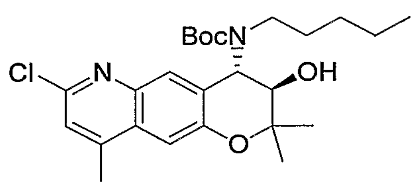
Synthesis Example 88

(*3R*,4S**)-7-chloro-2,2,9-trimethyl-6λ5-oxy-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride



This compound was synthesized by using the compound of Synthesis Example 52 similarly to the process of Synthesis Example 86.

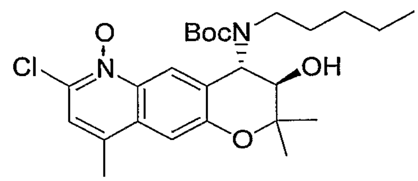
t-butyl (pentyl) [(*3R*,4S**)-7-chloro-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-yl] carbamate



MS(ESI$^+$)m/z; 463, 465 [M+1]$^+$

MS(ESI$^-$)m/z; 507, 509 [M+45]$^+$ (HCOOH adduct)

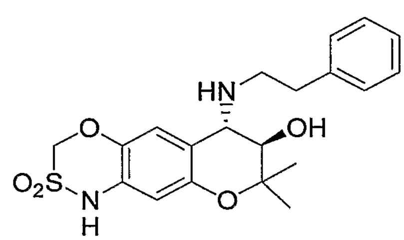
t-butyl (pentyl) [(*3R*,4S**)-7-chloro-3-hydroxy-2,2,9-trimethyl-6λ5-oxy-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-yl] carbamate



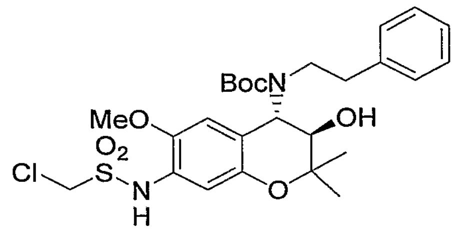
(2-steps yields: 23%).
MS(ESI$^+$)m/z; 479, 481 [M+1]$^+$
MS(ESI$^-$)m/z; 523, 525 [M+45]$^+$ (HCOOH adduct)

(*3R*,4S**)-7-chloro-2,2,9-trimethyl-6λ5-oxy-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride
(yield: 60%).
Pale yellow crystals
mp;226-230°C (decomposition)
^{1}H-NMR(DMSO-d_6) δ; 0.86(t, *J* = 6.3 Hz, 3H), 1.16(s, 3H), 1.27-1.29(m, 4H), 1.50(s, 3H), 1.60-1.72(m, 2H), 2.54(s, 3H), 2.86(brs, 1H), 3.07(brs, 1H), 4.07-4.10(m, 1H), 4.71(d, *J* = 8.5Hz, 1H), 6.51(d, *J* = 4.7 Hz, 1H), 7.47(s, 1H), 7.67(s, 1H), 9.04(s, 1H), 9.19(brs, 1H), 9.74(brs, 1H)
MS(ESI$^+$)m/z; 379, 381 [M+1]$^+$
MS(ESI$^-$)m/z; 423, 425 [M+45]$^+$ (HCOOH adduct)

Synthesis Example 89
(6S,7R*)*-8,8-dimethyl-6-[(2-phenylethyl)amino)]-1,6,7,8-tetrahydrochromeno[7,6-e][1,3,4]oxathiazin-7-ol 2,2-dioxide

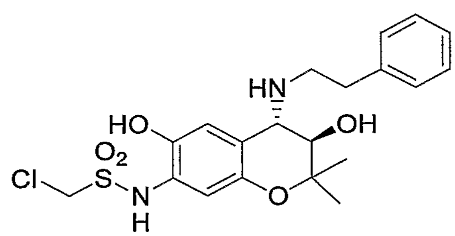


t-Butyl (2-phenylethyl)
[(*3R*,4S**)-7-{[(chloromethyl)sulfonyl]amino}-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-di hydro-2*H*-1-benzopyran-4-yl] carbamate



To a solution of *t*-butyl (2-phenylethyl) [(*3R**,*4S**)-7-amino-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyran-4-yl] carbamate described in Synthesis Example 71 (1.04 g, 2.35 mmol) in pyridine (1.90 mL, 23.5 mmol), chloromethanesulfonylchloride (0.31 mL, 3.52 mmol) was added, and the resulting mixture was stirred at room temperature for 10 hours. Upon the completion of the reaction, 1 mol/L aqueous hydrochloric acid solution (ca. 30 mL) was added thereto to adjust pH to about 7, and then the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium chloride solution, and dried over anhydrous sodium sulfate and concentrated. The resulting mixture was purified by column chromatography (hexane/ethyl acetate = 3/1) and the aimed product was obtained (yield: 81%).
Colorless oily product
LC/MS (ESI^+): 555$[M+1]^+$
LC/MS (ESI^-): 553$[M-1]^+$

1-Chloro-*N*-{(*3R**,*4S**)-3,6-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-7-yl} methanesulfonamide



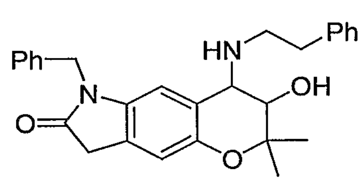
To a solution of *t*-butyl (2-phenylethyl) [(*3R**,*4S**)-7-{[(chloromethyl)sulfonyl]amino}-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyran-4-yl] carbamate (400 mg, 0.72 mmol) in dichloromethane (4.0 mL), 1 mol/L solution of boron tribromide in dichloromethane (3.61 mL, 3.61 mmol) was added on ice bath, and the resulting mixture was stirred at 0°C for 1 hour. Water was added, and the resulting mixture was further stirred for 30 minutes. The resulting solid was filtered off, washed with water and then with chloroform. The solid was dried at 60°C for 3 hours under reduced pressure, and the aimed product

was quantitatively obtained.
LC/MS (ESI$^+$): 441[M+1]$^+$
LC/MS (ESI$^-$): 439[M-1]$^+$

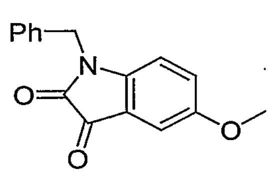
(6S,7R*)*-8,8-Dimethyl-6-[(2-phenylethyl)amino]-1,6,7,8-tetrahydrochromeno[7,6-e][1,3,4]oxathiazine-7-ol 2,2-dioxide

To a solution of 1-Chloro-*N*-{(*3R*,4S**)-3,6-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-7-yl} methanesulfonamide (220 mg, 0.50 mmol) in methanol (2.2 mL), 1 mol/L aqueous sodium hydroxide solution (1.00 mL, 1.00 mmol) was added, and the resulting mixture was stirred at room temperature for 3 hours. Then, the temperature was raised to 50°C, and the mixture was further stirred for 2 hours. Upon the completion of the reaction, the solution was cooled on standing, neutralized with saturated aqueous ammonium chloride solution, extracted 4 times with chloroform, and dried over anhydrous sodium sulfate. The solvent was distilled off and the aimed product was obtained (yield:37%).
Yellow solid
^{1}H-NMR ($CDCl_3$) δ: 1.13 (s, 3H), 1.44 (s, 3H), 2.54 (brs, 3H), 2.79-3.02 (m, 4H), 3.49 (d, *J* = 10.0 Hz, 1H), 3.59 (d, *J* = 10.0 Hz, 1H), 4.86 (s, 2H), 6.23 (s, 1H), 6.78 (s, 1H), 7.21-7.35 (m, 5H)
LC/MS (ESI$^+$): 405[M+1]$^+$
LC/MS (ESI$^-$): 403[M-1]$^+$

Synthesis Example 90
(±)-*trans*-6-Benzyl-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydro-pyrano[2,3-f]indol-7-one

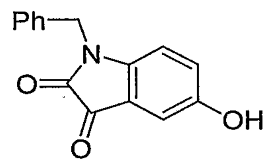


N-Benzyl-5-methoxyisatin



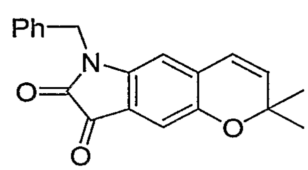
To a solution of 5-methoxyisatin (15.0 g, 84.7 mmol) in DMF (100 mL), sodium hydride (5.1 g, 127 mmol) and benzyl bromide (12.1 mL, 101.6 mmol) were added at 0°C, and the resulting mixture was stirred for 1 hour. Water was added thereto, and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated aqueous ammonium chloride solution and then with saturated sodium chloride solution, dried over anhydrous sodium sulfate, and concentrated to obtain the aimed product (yield: 96%).
Brown solid
^{1}H-NMR($CDCl_3$) δ; 3.77(s, 3H), 4.91(s, 2H), 6.67(d, J = 8.5 Hz, 1H), 7.0-7.1(m, 1H), 7.15 (m, 1H), 7.25-7.45(m, 5H)

N-Benzyl-5-hydroxyisatin



To a solution of *N*-benzyl-5-methoxyisatin (3.0 g, 11.2 mmol) in dichloromethane (60 mL), aluminum chloride (3.7 g, 28.1 mmol) was added, and the resulting mixture was stirred at 100°C for 1 hour. Water was added thereto, and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated sodium chloride solution, dried over anhydrous sodium sulfate, and concentrated to obtain the aimed product (yield: 78%).
Red solid
MS(ESI$^+$)m/z; 254 [M+1]$^+$
MS(ESI$^-$)m/z; 252 [M-1]$^+$

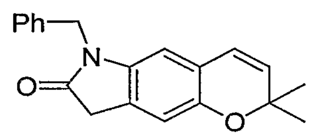
6-Benzyl-2,2-dimethyl-2*H*-pyrano[2,3-f]indole-7,8-dione



Under nitrogen stream, a solution of *N*-benzyl-5-hydroxyisatin (4.74 g, 18.7 mmol), potassium iodide (5.09 g, 31.8 mmol), potassium carbonate (5.17 g, 37.4 mmol), copper iodide (71 mg, 0.37 mmol) and 3-chloro-3-methyl-1-butyne (4.83 mL,

43.0 mmol) in DMF (47 mL) was stirred at 70°C for 2 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate, concentrated and purified by silica gel short column (chloroform).
1,2-dichlorobenzene (9 mL) was added and the resulting mixture was stirred ar 200°C for 30 minutes. After concentrating the reaction solution, the residue was purified by silica gel column (hexane/ethyl acetate = 5/1) to obtain the aimed product (yield: 8%).
Red oily product
MS(ESI$^+$)m/z; 320 [M+1]$^+$

6-Benzyl-2,2-dimethyl-2H-pyrano[2,3-f]indol-7-one



To a solution of 6-Benzyl-2,2-dimethyl-2*H*-pyrano[2,3-f]indole-7,8-dione (500 mg, 1.57 mmol) in DMF (5 mL), hydrazine monohydrate (2.5 mL) was added, and the resulting mixture was stirred at 100°C for 1.5 hour. Water was added thereto, and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated aqueous ammonium chloride solution and then with saturated sodium chloride solution, dried over anhydrous sodium sulfate, concentrated and purified by silica gel column (hexane/ethyl acetate = 3/1) to obtain the aimed product (yield: 65%).
Yellow amorphous product
MS(ESI$^+$)m/z; 306 [M+1]$^+$

(±)-*trans*-6-Benzyl-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydro-pyrano[2,3-f]indol-7-one

To 6-benzyl-2,2-dimethyl-2H-pyrano[2,3-f]indol-7-one (210 mg, 0.69 mmol) in chloroform-water mixed solution, sodium hydrogencarbonate (115 mg, 1.38 mmol) and *m*-chloroperbenzoic acid (237 mg, 1.38 mmol) were added, and the resulting mixture was stirred at room temperature for 3.5 hours. Aqueous sodium hydrogencarbonate solution and saturated aqueous sodium thiosulfate solution were added to the reaction solution, the resulting solution was extracted with chloroform, washed with saturated sodium chloride, dried over anhydrous sodium sulfate and

concentrated. 2-phenylethylamine (173 μL, 1.38 mmol), lithium perchlorate (73 mg, 0.69 mmol) and dioxane (1 mL) were added to the resulting residue, and the resulting mixture was stirred at 70°C for 2 hours. Water was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated sodium chloride solution, dried over anhydrous sodium sulfate, concentrated, purified by silica gel column (hexane/ethyl acetate = 1/1) and recrystallized with ethyl acetate to obtain the aimed product (2-steps yield: 16%).

Pale pink crystals

mp: 195°C (decomposition)

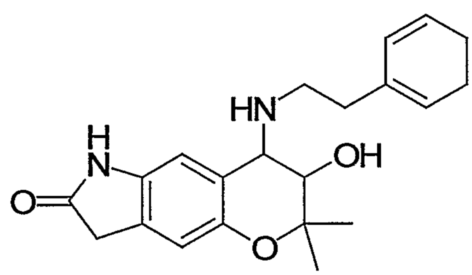
^{1}H-NMR($CDCl_3$) δ; 1.16(s, 3H), 1.45(s, 3H), 2.8-3.2(m, 4H), 3.51 (s, 2H), 3.59(d, *J* = 4.4Hz, 1H), 3.73(m, 1H), 4.75(d, *J* = 15.7Hz, 1H), 4.84 (d, *J* =15.7 Hz, 1H), 6.51 (s, 1H), 6.73 (s, 1H), 7.2-7.4(m, 10H).

MS(ESI^+)m/z; 443 $[M+1]^+$

MS(ESI^-)m/z; 441 $[M-1]^+$

Synthesis Example 91

(±)-*trans*-4-{[2-(cyclohexa-1,3-dien-2-yl)ethyl]amino}3-hydroxy-2,2-dimethyl-2,3,4,6-tetrahydro-pyrano[2,3-f]indol-7-one



Under nitrogen stream, sodium (90 mg, 3.91 mmol) was added to liquid ammonia (5 mL) at -78°C, and the resulting mixture was stirred. A solution of (±)-*trans*-6-benzyl-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydro-pyrano[2,3-f]indol-7-one (173 mg, 0.39 mmol) in THF (2 mL) was added dropwise at -45°C, and the resulting mixture was stirred for 15 minutes. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with water and then with saturated sodium chloride solution, dried over anhydrous magnesium sulfate, concentrated and purified by silica gel column (ethyl acetate) to obtain the aimed product (yield: 19%).

White solid
^{1}H-NMR($CDCl_3$) δ; 1.21(s, 3H), 1.49(s, 3H), 2.27(t, J = 6.9 Hz, 2H), 2.6-2.8(m, 4H),2.82-3.02(m, 2H), 3.44(m, 2H), 3.63(d, J = 4.4 Hz, 1H), 3.81 (d, J = 4.4 Hz, 1H), 5.54 (s, 1H), 5.74 (s, 2H), 6.72 (s, 1H), 6.86 (s, 1H), 8.78 (s, 1H).

[Preparation Examples]
Preparation Example 1
Tablet:

A compound according to the invention	10g
Lactose	260g
Microcrystalline cellulose	600g
Corn starch	350g
Hydroxypropyl cellulose	100g
CMC-Ca	150g
Magnesium stearate	30g
Total weight	1,500g

The aforementioned ingredients were mixed by a conventional method and then 10,000 sugar-coated tablets each containing 1 mg of the active ingredient per tablet were prepared.

Preparation Example 2
Capsule:

A compound according to the invention	10g
Lactose	440g
Microcrystalline cellulose	1,000g
Magnesium stearate	50g
Total weight	1,500g

The aforementioned ingredients were mixed by a conventional method and then filled into gelatin capsules to prepare 10,000 capsules each containing 1 mg of the active ingredient per capsule.

Preparation Example 3
Soft capsule:

A compound according to the invention	10g
PEG 400	479g
Saturated fatty acid triglyceride	1,500g
Peppermint oil	1g
Polysorbate 80	10g
Total weight	2,000g

The aforementioned ingredients were mixed by a conventional method and then filled into No. 3 soft gelatin capsules to prepare 10,000 soft capsules each containing 1 mg of the active ingredient per capsule.

Preparation Example 4

Ointment:

A compound according to the invention	1.0g
Liquid paraffin	10.0g
Cetanol	20.0g
White vaseline	68.4g
Ethylparaben	0.1g
1-menthol	0.5g
Total weight	100.0g

The aforementioned ingredients were mixed by a conventional method to obtain 1% ointment.

Preparation Example 5

Suppository:

A compound according to the invention	1g
Witepsol H15*	478g
Witepsol W35*	520g
Polysorbate 80	1g
Total weight	1,000g

(* trade name for triglyceride type compounds)

The aforementioned ingredients were melt-mixed by a conventional method, poured into suppository containers and cooled to solidify, and 1,000 suppositories (1g) each containing 1 mg of the active ingredient per suppository were prepared.

Preparation Example 6
Injection:

A compound according to the invention	1mg
Distilled water for injection	5mL

It is used by dissolving when applied.

[Pharmacological Test Example]
Effects on the effective refractory period
Method

Beagles were anesthetized with pentobarbital sodium and thoracotomy was done along the median line under a respirator and the incision was made on the pericardium to expose the heart. An electrocardiogram (ECG) was recorded using bipolar electrodes attached to the surface of the right atrial free wall, right atrial auricle, and right ventricular free wall. The vagal nerves were stimulated using an electrostimulation device with Nichrome wires inserted into the vagal nerves in the neck bilaterally. The conditions for electrostimulation to the vagal nerves were set such that the RR intervals on ECG were prolonged by about 100msec compared with those before the stimulation was started.

Atrial and ventricular effective refractory periods were determined by S1-S2 extrastimulus technique at basic cycle length of 300 msec during bilateral vagal nerve stimulation, using programmable electric stimulator. A train of 10 basic stimuli(S1) was followed by a premature extrastimulus (S2) at 2 times diastolic threshold. The S1-S2 interval was successively decreased by 2 msec, and the effective refractory period was defined as the point at which S2 failed to produced a propagated response.

For evaluation of drug effects, the atrial and ventricular effective refractory periods were determined before drug administration, then respective compound was administrated intravenously at the dose of 0.3 mg/kg or 0.6 mg/kg, and the atrial and ventricular effective refractory periods were determined from 5 minutes after the administration.

The results were shown as the prolongation time on the atrial and ventricular effective refractory periods, i.e. [effective refractory period after drug administration] - [effective refractory period before drug administration] (msec).

Results

The compounds of the present invention exhibited the prolongation effect on the effective refractory period selective for atrium as shown in Table below.

Table

Synthesis Example No.	Dose (mg/kg) (mg/kg)	Atrial Refractory Period (msec)
2	0.6	21
4	0.6	30
6	0.6	20
7	0.6	25
8	0.6	23
14	0.3	27
18	0.3	27
19	0.3	26
23	0.3	22
24	0.3	23
25	0.3	27
26	0.3	24
27	0.3	32
41	0.3	21
47	0.3	24
48	0.3	23
52	0.3	28
53	0.3	30
58	0.3	28
59	0.3	22
60	0.3	22
61	0.3	20
63	0.3	23
69	0.3	37
71	0.3	31
73	0.3	31
74	0.3	25
77	0.3	25

Effects of the invention

The compounds according to the present invention exhibit the prolongation effect on the effective refractory period selective for atrium, thus can be used as an anti-atrial fibrillation agents and an supraventricular antiarrhythmic agent, and are useful as pharmaceuticals. Further, since the compounds according to the present invention have small influence on ventricle, they can contribute to safe treatments of aforementioned arrhythmic conditions.